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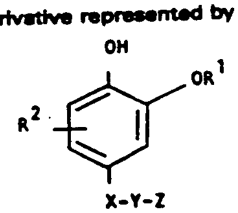
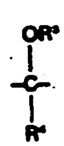
(54) **Catechol derivatives, their production and intermediates therefor, and pharmaceutical compositions containing them.**

(57) A catechol derivative represented by the formula



wherein R^1 represents a hydrogen atom or a C_1 to C_4 alkyl group; R^2 represents a hydrogen atom or a halogen atom; X represents a straight chain or branched alkylene group having 1 to 15 carbon atoms or a vinylene group; Y represents a carbonyl group or a group represented by



(wherein R^3 and R^4, which may be the same or different, each represents a hydrogen atom or a C_1 to C_4 alkyl group) and Z represents a hydrogen atom, a straight chain or branched alkyl group having 1 to 15 carbon atoms or a cycloalkyl group; the sum of the carbon atoms of said X and Z being at least 3.

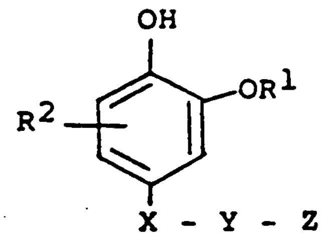
The compounds of this invention are useful for the prophylaxis and treatment for various allergic diseases, ischemic heart diseases an inflammations caused by slow reacting substance of anaphylaxis (SRS-A), since the compounds inhibit very potently the formation and release of SRS-A.

Croydon Printing Company Ltd.

As an inhibitor of histamine release, disodium cromoglycate (DSCG) is well known and as an inhibitor of actions induced by histamine, various anti-histamics are commercially available. On the other hand, SRS-A is known as a slow reactive and long acting chemical mediator while histamine is a rapid acting and short acting chemical mediator, and it has recently been recognized that SRS-A is a mixture of Leukotriens C_4, D_4 and E_4 the structures of which have been clarified by Dr. Samuelsson . SRS-A, i. e., Leukotriens are lipoxigenase products of polyunsaturated fatty acids (in particular, arachidonic acid) and it has been reported that SRS-A has various activities such as enhancement of mucus production, reduction of mucociliary transport, coronary artery constrictor action, reduction of cardiac contractility, etc., in addition to the actions in the above-described allergic reactions. Only a few materials have been known as the medicaments for inhibiting the production and release of SRS-A or combating the actions of SRS-A, and they have not yet been clinically used.

We have found the compounds of this invention as defined hereinafter and that they are useful as medicaments capable of strongly inhibiting the formation and release of SRS-A and/or of combating the action of SRS-A.

The compounds of the invention are catechol derivatives represented by the general formula (I)



(I)

wherein R^1 represents a hydrogen atom or a lower alkyl group; R^2 represents a hydrogen atom or a halogen atom; X represents a straight chain or branched alkylene group having 1 to 15 carbon atoms or a vinylene group; Y represents a carbonyl group or a group shown by the formula $-\underset{R^4}{\overset{OR^3}{\overset{|}{\underset{|}{C}}}}-$ (wherein R^3 and R^4, which may be the same or different, each represents a hydrogen atom or a lower alkyl group); and Z represents a hydrogen atom, a straight chain or branched alkyl group having 1 to 15 carbon atoms or a cycloalkyl group; the sum of the carbon atoms of said X and Z being at least 3.

The term "lower alkyl group" herein means a straight chain or branched alkyl group having 1 to 5 carbon atoms, such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, a pentyl group etc.

The "halogen atom" shown by R^2 in the foregoing general formula may be a chlorine atom, a bromine atom, an iodine atom or a fluorine atom.

The "straight chain alkylene group" shown by X includes a methylene group, an ethylene group, a propylene group, a pentanylene group (or pentamethylene group, $-(CH_2)_5-$), a hexanylene group (hexamethylene group, $-(CH_2)_6-$), a heptanylene group (heptamethylene group, $-(CH_2)_7-$), a nonanylene group (nonamethylene group, $-(CH_2)_9-$), an undecanylene gorup (undecamethylene group, $-(CH_2)_{11}-$), a tridecanylene group (tridecametylene group, $-(CH_2)_{13}-$), a tetradecanylene group (tetradeca-methylene group, $-(CH_2)_{14}-$), a pentadecanylene group (pentadecamethylene group, $-(CH_2)_{15}-$), etc. Also, the "branched alkylene group" shown by X includes the above-described straight chain groups having a lower alkyl group of 1 to 5 carbon atoms at an optional position thereof. Specific examples of the branched alkylene group are a propylene group ($-\underset{\underset{CH_3}{|}}{C}HCH_2-$), an ethylethylene group ($-CH_2\underset{\underset{CH_2CH_3}{|}}{C}H-$), etc.

Examples of the group shown by $-\overset{\overset{OR^3}{|}}{\underset{\underset{R^4}{|}}{C}}-$ represented by Y in the foregoing general formula are a hydroxymethylene

group, a methoxymethylene group, a methylhydroxymethylene group ($-\overset{\displaystyle OH}{\underset{\displaystyle CH_3}{C}}-$), a methylmethoxymethylene group ($-\overset{\displaystyle OCH_3}{\underset{\displaystyle CH_3}{C}}-$), an ethylhydroxymethylene group ($-\overset{\displaystyle OH}{\underset{\displaystyle CH_2CH_3}{C}}-$), etc.

The "straight chain alkyl group" shown by Z in the foregoing general formula includes a propyl group, a pentyl group, a hexyl group, an octyl group, a nonyl group, a decyl group, a undecyl group, etc. Also, the "branched alkyl group" shown by Z includes alkyl groups having a lower alkyl group of 1 to 5 carbon atoms at an optional position thereof and specific examples are an isopropyl group, an isobutyl group, a 1-methylhexyl group, a 1-ethylpentyl group, a 1,5-dimethylhexyl group, a 2,3,5-trimethylheptyl group, a 4-propylnonyl group, a 1-hexylpeptyl group, etc. Also, the "cycloalkyl group" shown by Z includes a cyclopentyl group, a cyclohexyl group, etc.

When X represents a branched alkylene group, Y represents a group shown by $-\overset{\displaystyle OR_3}{\underset{\displaystyle R_4}{C}}-$, and/or Z represents a branched alkyl group, with different alkyl groups on the branch carbon atom(s), the compound of this invention shown by the above-described general formula has at least one asymmetric carbon atom. Thus, the desired compounds of this invention include each separate steroisomer based on the asymmeteric carbon atom and mixtures of these steroisomers.

Since the compounds of this invention shown by general formula (I) inhibit the formation and release of SRS-A, the compounds are useful for the prophylaxis and treatment of various allergic diseases (e. g., bronchial asthma, allergic rhinitis, and urticaria) and ischemic heart diseases and inflamations caused by SRS-A.

Pharmacological experiment

A) Passive peritoneal anaphylaxis(PPA) in rats

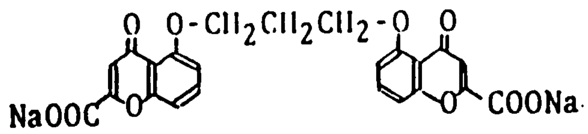
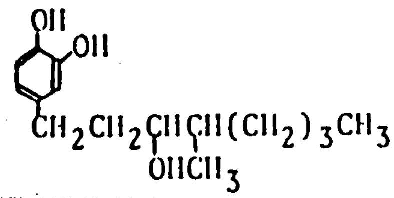
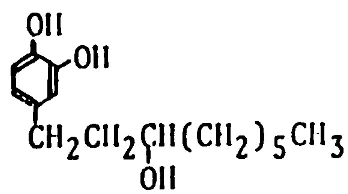
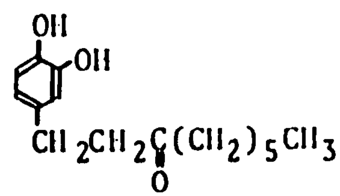
The method was based on that of Orange *et al*[1]. Briefly, male Wister rats weighing 275 to 325 g (Shizuoka Exp. Animal Agric, Coop. Assoc.) were sensitized by intraperitoneally (i.p.) injecting 5 ml of diluted (40-fold) mouse anti-DNP reaginic serum (PCA titer: 1280). After 4 hr, 5 ml of Tyrode solution containing 250 μg heparin and 2 mg DNP-BSA was injected i.p. Test drugs (100 μg/kg) were dissolved in 0.6 ml of saline and injected i.p. 30 sec before antigen administration. Five min. later, the rats were decapitated and the peritoneal fluid was collected by opening the peritoneal cavity into polycarbonate tubes in ice. The supernatant was separated for bioassay from the cellular residue by centrifugation at 2000 rpm for 5 min at 4°C.

Histamine and SRS-A were assayed using isolated guinea-pig ileum in the presence of 10^{-7}M FPL-55712 and 10^{-6}M mepyramine, respectively, in addition to 5×10^{-7} M atropine.

One unit of SRS-A refers to the concentration required to produce a contraction of the guinea-pig ileum equal in amplitude to that produced by 5 ng histamine base in that assay.

1) Orange *et al* (1970) J. Immunol. 105, 1087-1095

Table 1

		Drug	Rat PPA (100 μg/kg i.p.) Inhibition (%)	
ALT-No	Example	Formula	Histamine	SRS-A
-	-	 (DSCG)	75.2[1)]	46.6[1)]
18	1		37.8	76.6
28	2		5.2	57.3
27	3		22.6	53.9

1) The results represent the mean of 3 rats.

Table 1 (Continue. 1)

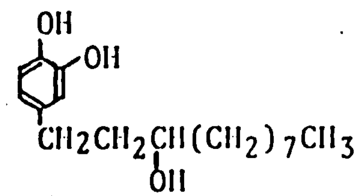
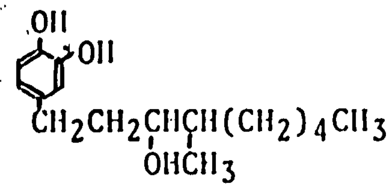
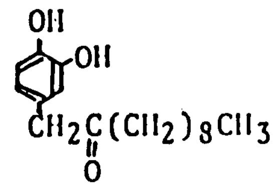
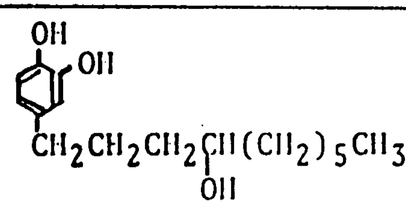
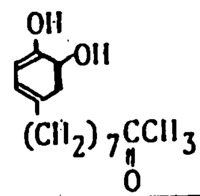
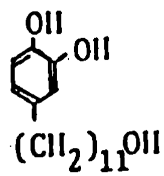
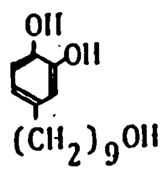
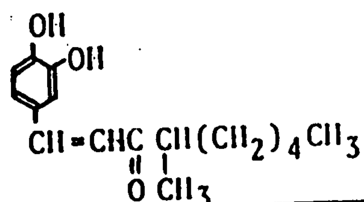
		Drug	Rat PPA (100 μg/kg i.p.) Inhibition (%)	
ALT-No	Example	Formula	Histamine	SRS-A
70	9		21.6	53.6
69	11		17.6	66.6
82	14		32.7	58.9
52	15		18.4	46.2

Table 1 (Continued 2)

		Drug	Rat PPA (100 μg/kg i.p.) Inhibition (%)	
ALT-No	Example	Formula	Histamine	SRS-A
103	20		17.9	62.8
118	23		10.7	69.6
117	25A		-8.3	43.9
77	29		-32.4	38.2

As shown in Table 1, the compounds of this invention more effectively inhibited the antigen-induced SRS-A release than histamine release, whereas DSCG inhibited the histamine release in a relatively selective manner.

These results suggest that there is a difference in action between the compounds of this invention and DSCG.

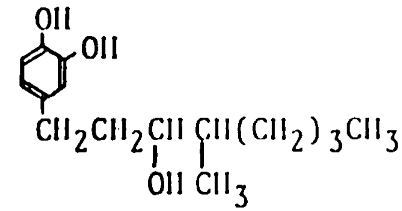
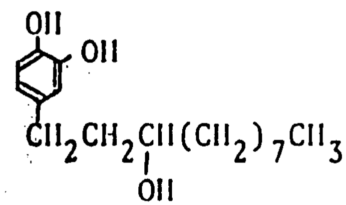
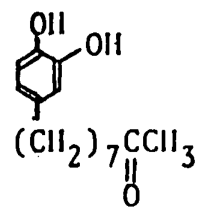
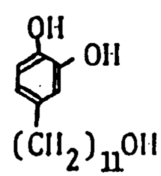
B) Assay of 5-lipoxygenase and cyclooxygenase

The method was based on that of Koshihara *et al*[1]. In the case of assay of 5-lipoxygenase activity, enzyme fraction from mastocytoma P-815 cells (10^7 cells/ml) was incubated with 0.2 μCi [1-^{14}C]-arachidonic acid (56.9 Ci/mol), 0.8 mM $CaCl_2$, 2 x 10^{-5}M indomethacin and various concentrations of test drugs at 37°C for 5 min. In the case of assay of cyclooxygenase activity, $CaCl_2$ and indomethacin were omitted from the above incubation mixture and incubation was performed at 37°C for 7 min. Both reactions were terminated by adjusting the pH of the mixture to 3.0 with HCl. After extraction of the products with 8 volume ethyl acetate, each extract was concentrated and applied to TLC plate. For the separation of HETEs and prostaglandins, thin-layer chromatography was carried out using solvent system: petroleum ether/diethyl ether/acetic acid (50:50:1) and ethyl acetate/2,2,4-trimethylpentane/acetic acid/water (11:5:2:10, upper phase), respectively. Radioactive spots were detected by autoradiography and scraped off

and counted using liquid scintillation spectrometer. The activities of 5-lipoxygenase and cyclooxygenase were expressed as the sum of radioactivities due to 5-HETE and 5,12-diHETE and due to PGD_2, PGE_2 and $PGF_{2\alpha}$, respectively. The IC 50 values were calculated by Probit method.

1) Koshihara _et_ _al_. (1982) FEBS Letters __143__, 13-16.

Table 2

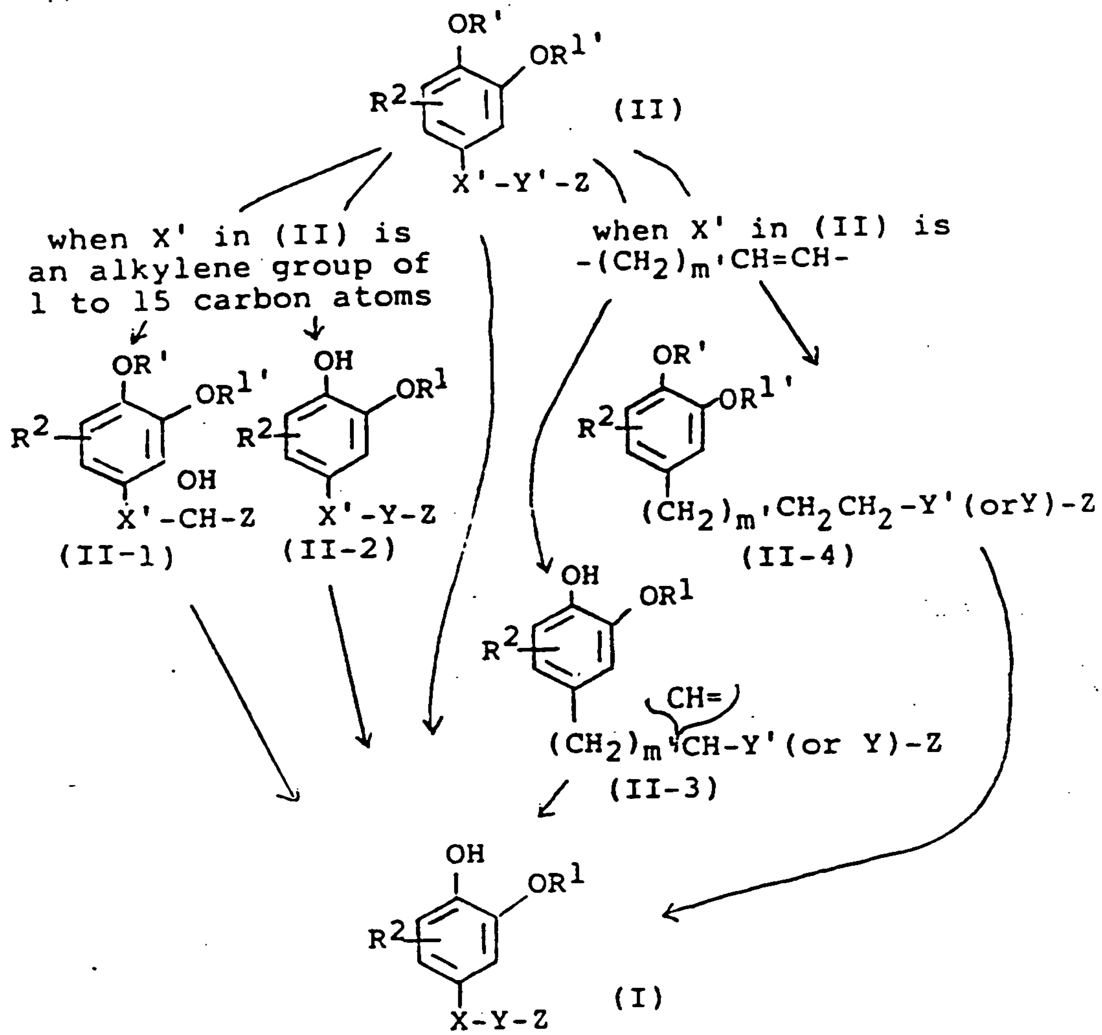
Drug			IC 50 (μM)	
ALT No.	Example	Formula	5-Lipoxygenase	Cyclooxygenase
18	1		0.30	Enhanced
70	9		0.10	>10
103	20		0.23	>10
118	23		0.054	>10

The compounds of this invention dose-dependently inhibited the formation of 5-lipoxygenase products in doses between 0.01 to 10 μM; their IC 50 values are shown in Table 2. On the contrary, at 10 μM they showed weak inhibition or enhancement of the formation of cyclooxygenase products.

These results indicate that the compounds of this invention specifically inhibit 5-lipoxygenase.

The compounds of this invention shown by general formula (I) can be stably administered orally or parenterally by themselves or as medicament compositions [e.g., tablets, capsules (including soft capsules, microcapsules, etc.,), powders, granules, pills, ointments, syrups, injections, inhalators, plasters, etc.,] mixed with known pharmaceutically allowable carriers, excipients, etc. The dose thereof depends upon the subject to be treated, the manner of administration, the state of the disease, etc., but is ordinarily 0.1 to 500 mg per day per adult, and it is appropriate to administer the compound orally or parenterally two or three times per day.

The compounds of this invention shown by general formula (I) can be prepared by the methods shown in the following reaction formulae:



wherein R^1, R^2, X, Y, and Z have the same significance as defined above; R' represents a protective group for the hydroxy group capable of being easily removed; $R^{1'}$ represents a protective group for the hydroxy group capable of being easily removed or a lower alkyl group; X' represents a straight chain or branched alkylene group having 1 to 15 carbon atoms, an alkenylene group represented by the formula $-(CH_2)_{m'}CH=CH-$ (wherein m' represents 0 or an integer of 1 to 13), a group represented by the formula $-\overset{O}{\overset{\|}{C}}-(CH_2)_{m''}-$ (wherein m" represents an integer of 1 to 14), or a group represented by the

general formula $-\overset{OH}{\overset{|}{C}}H-(CH_2)_{m''}-$ (wherein m" has the same significance as above); said $-(CH_2)_{m'}-$ and $-(CH_2)_{m''}-$ may be branched; Y' represents a carbonyl group or a group shown by $-\overset{OR^{3'}}{\overset{|}{\underset{\underset{R^4}{|}}{C}}}-$ ($R^{3'}$ and R^4, which may be the same or different, each represents a hydrogen atom or a lower alkyl group; said $R^{3'}$ may mean a protective group for a hydroxy group; the sum of said X' and Z being at least 3.

In the above-described methods, a 1-(3-hydroxy(or 3-lower alkoxy)-4-hydroxyphenyl)alkane of general formula (I) is produced by reducing or hydrolyzing the corresponding 1-(3,4-di-substituted phenyl)alkane or 1-(3,4-disubstituted phenyl)alkene. The reduction includes (a) the removal of the protective group for the hydroxy group, (b) the the reduction of a carbonyl group ($-\overset{O}{\overset{\|}{C}}-$) shown by Y' into a hydroxymethylene group ($-\overset{OH}{\overset{|}{C}}H-$), and (c) the saturation of an unsaturated bond (alkenylene group $\longrightarrow$ alkylene group).

The reduction may be performed in any order. Also, by properly selecting the conditions, the reduction may be a partial reduction.

The removal of the protective group for the hydroxy group of the foregoing reduction (a) differs according to the kind of the protective group. In the production method of the compounds of this invention, a benzyl group, a p-methoxybenzyl group, a benzyloxycarbonyl

group, a methoxymethyl group, an acetyl group, or a benzoyl group may for example be employed as a protective group and the removal of the protective group is usually performed by catalytic reduction using palladium-carbon as a catalyst, reduction by metallic sodium in liquid ammonia, acid hydrolysis or alkali hydrolysis.

The conversion of a carbonyl group into a corresponding hydroxymethylene group of reduction (b) may be by chemical reduction using aluminum lithium hydride ($LiAlH_4$), sodium boron hydride ($NaBH_4$), etc., or catalytic reduction using palladium-carbon, etc.

Also, the reduction of an alkenylene group ($-(CH_2)_{m'}CH=CH-$) into an alkylene group ($-(CH_2)_{m'}CH_2CH_2-$) of the reduction (c) may be by catalytic reduction using palladium-carbon, Raney nickel catalyst, platinum black, etc.

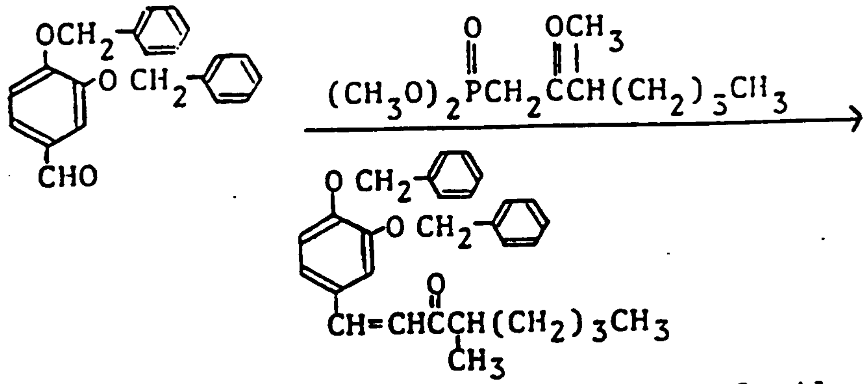
For the production methods of the compounds of this invention shown by general formula (I), there are further a halogenation of a benzene ring, a lower alkoxylation of a hydroxy group, etc. These reactions can be performed in ordinary manner.

The following Examples are intended to illustrate the compounds of this invention shown by formula (I) and the production methods of the compounds but not to limit in any way.

In addition, since the raw materials used in the following Examples include novel compounds, the production methods of these compounds are explained by

the following reference Examples.

Reference Example 1 (a)

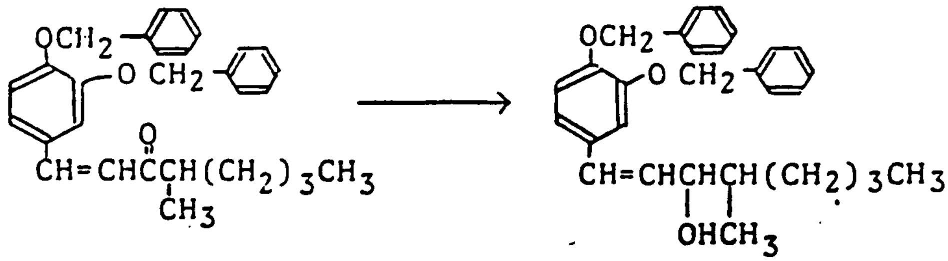


While stirring a mixture of 400 mg of oily sodium hydride (60%) and 50 ml of 1,2-dimethoxyethane, a mixture of 2.36 g of dimethyl (3-methyl-2-oxo)heptyl phosphonate and 5 ml of dimethoxyethane was added dropwise to the mixture at 20° to 25°C. Then, after stirring the resultant mixture for 2 hours at room temperature, the reaction mixture was cooled to 5° to 7°C and a mixture of 2.3 g of 3,4-dibenzyloxybenzaldehyde and 5 ml of dimethoxyethane was added dropwise to the reaction mixture.

After stirring the reaction mixture for 2 hours at room temperature, 300 ml of water was added to the reaction mixture and the product was extracted with 50 ml of toluene-n-hexane (1 : 1). The extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to provide a sticky residue . The residue was applied to silica gel (70 ml) column chromatography and eluted with a mixture of n-hexane and ether (4 : 1) to provide 1.2 g of 1-(3,4-dibenzyloxyphenyl)-4-methyl-1-octen-3-one.

~~Melting point 62 64°C.~~

Reference Example 1 (b) (Raw material in Example 1)

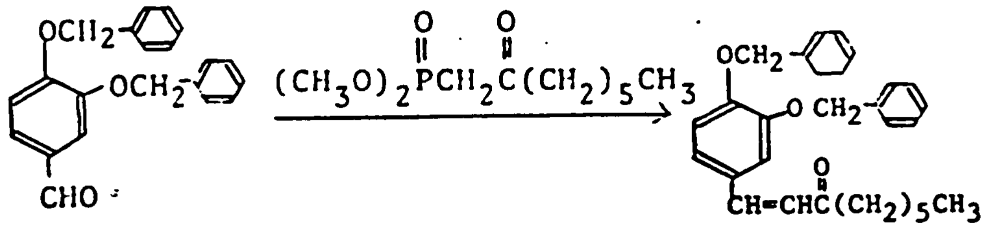


To a mixture obtained by adding 0.1 g of lithium aluminum hydride to 20 ml of ether was added 0.55 g of 1-(3,4-dibenzyloxyphenyl)-1-octen-3-one under ice-cooling and the mixture was stirred for one hour at room temperature. To the reaction mixture was gradually added 10 ml of an aqueous 10% hydrochloric acid solution and the ether layer was collected, washed with water, and concentrated under reduced pressure to provide a solid product. By washing the product with a mixture of ether and n-hexane (1 : 3), 0.4 g of 1-(3,4-dibenzyloxyphenyl)-4-methyl-1-octen—3-ol was obtained.

Melting point 77- 78°C.

Then, by following the same procedures as in Reference Example 1 (a) and (b), the following compounds of Reference Example 2 (a) and (b) were obtained and by following the same procedure as in Reference Example 1 (a), the following compounds of Reference Examples 3 to 7 were obtained.

Reference Example 2 (a) (Raw material in Example 3)



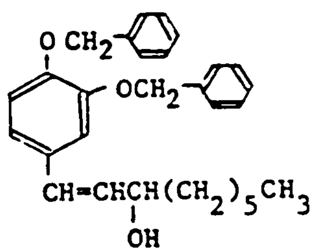
1-(3,4-Dibenzyloxyphenyl)-1-nonen-3-one. Melting point 78 - 80°C.

Elemental analysis for $C_{29}H_{32}O_3$:

	C	H
Calculated:	81.27%	7.53%
Found:	81.21%	7.65%

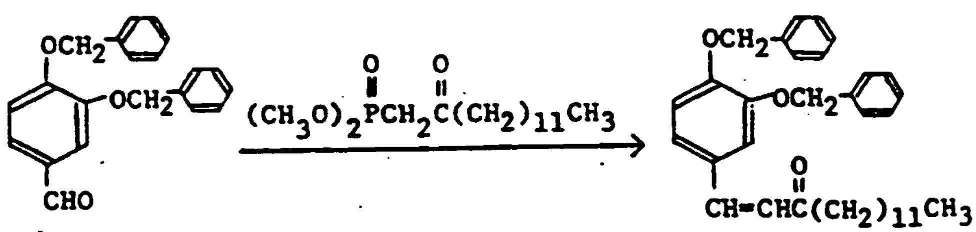
Reference Example 2 (b) (Raw material in Example 2)

(Using the compound obtained in the above step (a))



1-(3,4-Dibenzyloxyphenyl)-1-nonen-3-ol. Melting point 90 - 92°C.

Reference Example 3 (Raw material in Example 4)



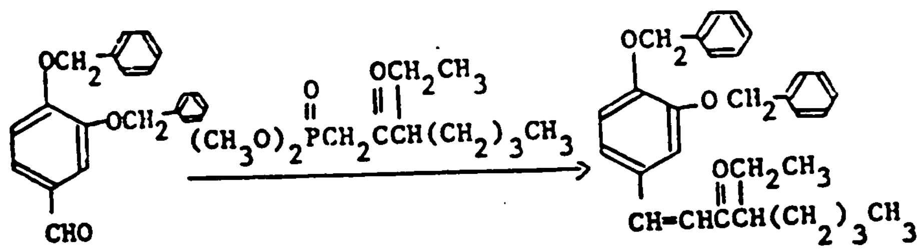
1-(3,4-Dibenzyloxyphenyl)-1-pentadecen-3-one. Melting point 81 - 82°C.

0125919

Elemental analysis for $C_{35}H_{44}O_3$:

	C	H
Calculated:	81.99%	8.65%
Found:	81.78%	8.81%

Reference Example 4 (Raw material in Example 5)



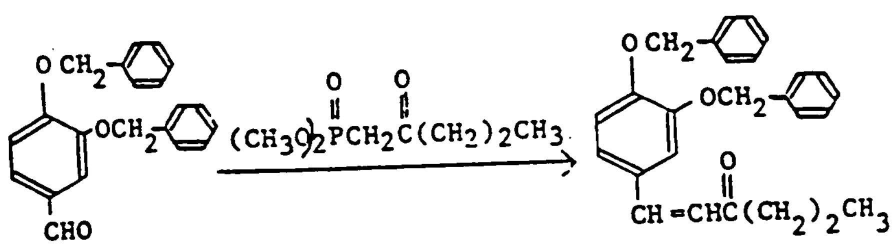
1-(3,4-Dibenzyloxyphenyl)-4-ethyl-1-octen-3-one.

Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm.)

0.86(6H), 1.1-1.9(8H), 2.65(1H), 5.15(4H), 6.4-7.6(15H).

Reference Example 5 (Raw material in Example 6)



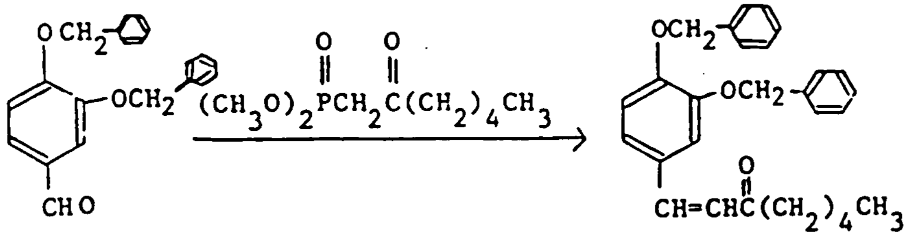
1-(3,4-Dibenzyloxyphenyl)-1-hexen-3-one.

Melting point 82 - 84°C

Elemental analysis for $C_{26}H_{26}O_3$:

	C	H
Calculated:	80.80%	6.78%
Found:	80.80%	6.81%

Reference Example 6 (Raw material in Example 7)



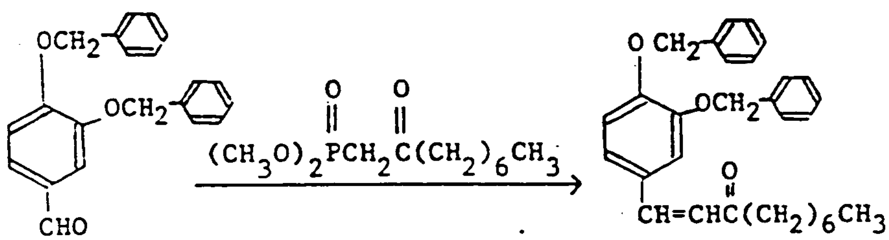
1-(3,4-Dibenzyloxyphenyl)-1-octen-3-one.

Melting point 71 - 73°C

Elemental analysis for $C_{28}H_{30}O_3$:

	C	H
Calculated:	81.13%	7.29%
Found:	80.91%	7.47%

Reference Example 7 (Raw material in Example 8)



1-(3,4-Dibenzyloxyphenyl)-1-decen-3-one.

Melting point 73 - 75°C

Elemental analysis for $C_{30}H_{34}O_3$:

	C	H
Calculated:	81.41%	7.74%
Found:	81.26%	7.97%

In addition, the properties and production methods of dimethyl 2-oxoalkylphosphonates used in the above reference examples are shown below.

Method A:

$$(CH_3O)_2\overset{O}{\overset{\|}{P}}CH_3 + CH_3CH_2CH_2COOC_2H_5 \xrightarrow{n\text{-}BuLi} (CH_3O)_2\overset{O}{\overset{\|}{P}}CH_2\overset{O}{\overset{\|}{C}}CH_2CH_2CH_3$$

In 65 ml of anhydrous tetrahydrofuran was dissolved 12.75 g of dimethyl methylphosphonate and the solution was cooled below -70°C. Then, while stirring the solution under nitrogen stream, 67 ml of a hexane solution (10 v/w%) of n-butyl lithium (n-BuLi) cooled below -70°C was added dropwise to the solution over a 30 minute period and the mixture was stirred for 15 minutes at the same temperature. Then, a solution of 5.8 g of ethyl n-butyrate in 15 ml of anhydrous tetrahydrofuran cooled below -70°C was added dropwise to the mixture over a 15 minute period and the resultant mixture was stirred for 1.5 hours below -70°C and then for 2 hours at room temperature.

The reaction mixture thus obtained was ice-cooled, mixed with 10 ml of glacial acetic acid, and the solvent was distilled off from the mixture under reduced pressure. To the residue was added 50 ml of water and the product was extracted thrice each time with 50 ml of ethyl ether. The extracts were combined with each other and washed twice each time with 20 ml of a saturated aqueous sodium chloride solution. After drying the extract by anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was vacuum-distilled to provide

9.7 g of dimethyl 2-oxopentylphosphonate.

Boiling point 95-97°C/0.9 mm Hg.

By following the procedure as in Method A, the phosphonate compounds having the following formulae were prepared.

	Boiling point
$(CH_3O)_2\overset{O}{\overset{\|}{P}}CH_2\overset{O}{\overset{\|}{C}}(CH_2)_4CH_3$	113-115°C/0.8 mm Hg
$(CH_3O)_2\overset{O}{\overset{\|}{P}}CH_2\overset{O}{\overset{\|}{C}}(CH_2)_6CH_3$	129-132°C/0.9 mm Hg
$(CH_3O)_2\overset{O}{\overset{\|}{P}}CH_2\overset{O}{\overset{\|}{C}}\overset{CH_2CH_3}{\overset{\mid}{C}H}(CH_2)_3CH_3$	126-128°C/0.85 mm Hg
$(CH_3O)_2\overset{O}{\overset{\|}{P}}CH_2\overset{O}{\overset{\|}{C}}\overset{CH_3}{\overset{\mid}{C}H}(CH_2)_3CH_3$	104-108°C/0.25 mm Hg
$(CH_3O)_2\overset{O}{\overset{\|}{P}}CH_2\overset{O}{\overset{\|}{C}}(CH_2)_5CH_3$	120-123°C/0.4 mm Hg

Method B:

$$(CH_3O)_2\overset{O}{\overset{\|}{P}}CH_2\overset{O}{\overset{\|}{C}}(CH_2)_{11}CH_3$$

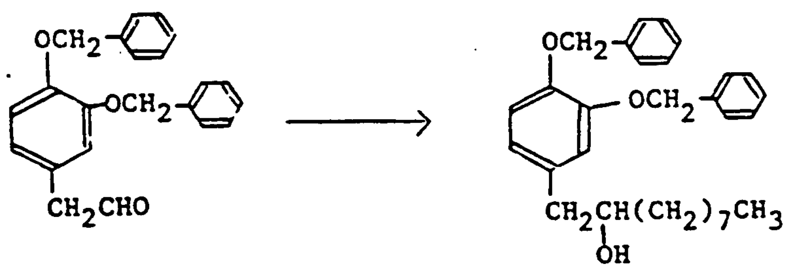
A mixture of 2.5 g of dimethyl methylphosphonate and 15 ml of anhydrous tetrahydrofuran was cooled below -70°C and 13.5 ml of a hexane solution (10 v/w%) of n-butyl lithium cooled below -70°C was added dropwise to the mixture with stirring under nitrogen stream over a 30 minute period followed by stirring for 15 minutes at the same temperature. Then, a mixture of 2.4 g of ethyl tridecanoate and 5 ml of anhydrous tetrahydrofuran was added dropwise to the mixture over a 10 minute period and the resultant mixture was stirred for 1 hour at a temperature below -70°C and then for 2 hours at

room temperature.

The reaction mixture thus obtained was ice-cooled, mixed with 2 ml of glacial acetic acid, the mixture was concentrated under reduced pressure, and then extracted thrice each time with 10 ml of ethyl ether. The extracts were combined, washed with a saturated aqueous sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to provide an oily product. The oily produce was applied to silica gel (40 ml) column chromatography and eluted with ethyl ether to provide 2.5 g of dimethyl 2-oxo-tetradecanoylphosphonate.

Boiling-point 37-38^{o}C.

Reference Example 8 (Raw material in Example 13)



After gradually adding 0.5 g of 3,4-dibenzyloxyphenyl acetaldehyde to 10 mg of an ether solution of n-octylmagnesium bromide obtained from 0.12 g of magnesium and 0.97 g of n-octyl bromide, the mixture was stirred for 30 minutes at room temperature. To the reaction mixture thus obtained was added 10 ml of an aqueous 5% hydrochloric acid solution and after stirring the mixture, the ether layer was collected. The ether solution was washed with water, dried over anhydrous magnesium sulfate, and concentrated under

reduced pressure to provide 0.5 g of 1-(3,4-dibenzyloxyphenyl)-2-decanol.

Melting point 55-57°C (n-hexane).

Elemental analysis for $C_{30}H_{38}O_3$:

	C	H
Calculated:	80.54%	8.78%
Found:	80.68%	8.58%

By following the procedure as in Reference Example 8, the following compounds (Reference Examples 9 to 11) were prepared. The names of these compounds are shown below together with the melting points and/or nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm).

Reference Example 9 (Raw material in Example 16)

1-(3,4-Dibenzyloxyphenyl)-2-nonanol.

0.7-1.6(15H), 2.57(2H), 3.63(1H), 5.08(4H), 6.5-7.5(13H).

Reference Example 10 (Raw material in Example 17)

1-(3,4-Dibenzyloxyphenyl)-2-undecanol.

Melting point 55-57°C.

0.7-1.6(19H), 2.57(2H), 3.59(1H), 5.07(4H), 6.5-7.5(13H).

Elemental analysis for $C_{31}H_{40}O_3$:

	C	H
Calculated:	80.83%	8.75%
Found:	80.83%	8.89%

Reference Example 11 (Raw material in Example 18)

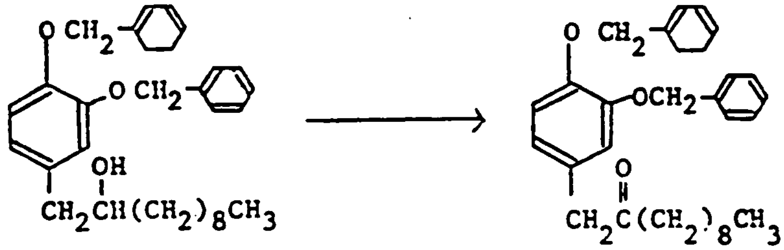
2-(3,4-Dibenzyloxyphenyl)-1-cyclohexyl-1-ethanol.

Melting point 73-75°C.

Elemental analysis for $C_{28}H_{32}O_3$:

	C	H
Calculated;	80.73%	7.74%
Found:	80.65%	7.80%

Reference Example 12 (Raw material in Example 14)



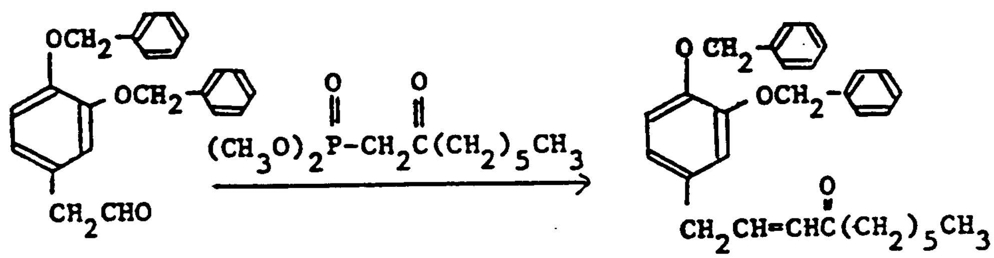
To a mixture of 15 ml of methylene chloride and 1.2 ml of pyridine was gradually added 2 g of chromic anhydride under cooling to 0°C to -5°C and after stirring the mixture for 10 minutes at 0° to -3°C, a solution of 0.9 g of 3,4-dibenzyloxyphenyl-2-undecanol in 3 ml of methylene chloride was added to the mixture. After further stirring the mixture for 20 minutes at 0° to 10°C, the supernatent methylene chloride solution was concentrated under reduced pressure. The residue was applied to silica gel column chromatography and eluted with toluene to provide 0.8 g of 1-(3,4-dibenzyloxyphenyl)-2-undecanone..

Melting point 68°C.

Elemental analysis for $C_{31}H_{38}O_3$:

	C	H
Calculated:	81.18%	8.35%
Found:	81.13%	8.28%

Reference Example 13 (Raw material in Example 15)



To a solution obtained by adding 200 mg of oily sodium hydride (60%) to a mixture of 25 ml of 1,2-dimethoxyethane and 10 ml of dimethyl sulfoxide was added dropwise a mixture of 1.2 g of diemthyl 2-oxo-octylphosphonate and 3 ml of dimethoxyethane at 20 to 25°C. Thereafter, the mixture was stirred for 2 hours at room temperature and after adding thereto small pieces of dry ice, the mixture was further stirred for 5 minutes. To the reaction mixture was added 200 ml of water and the product was extracted with toluene. The extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was applied to silica gel column chromatography and eluted with a mixture of toluene and ethyl acetate (10 : 1) to provide 0.5 g of 1-(3,4-dibenzyloxyphenyl)-2-decen-4-one as an oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS

internal standard, ppm)

0.7-1.8(11H), 2.42(2H), 3.24(2H), 5.09(4H), 6.0-7.7(15H)

Reference Example 14 (Raw material in Example 19)

By following the procedure as in Reference Example 13, 1-(3,4-dibenzyloxyphenyl)-3-decen-5-one was obtained from 1-(3,4-dibenzyloxyphenyl)propionaldehyde and dimethyl 2-oxohexylphosphonate.

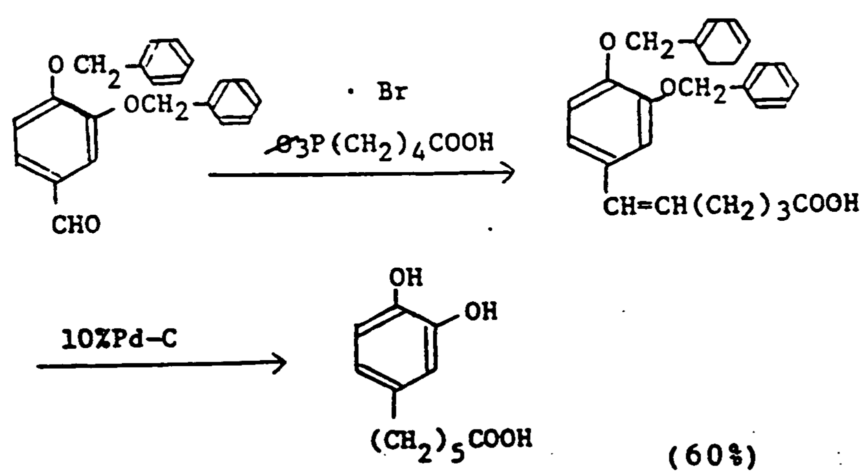
Melting point 38-39°C

Elemental analysis for $C_{30}H_{34}O_3$:

	C	H
Calculated:	81.41%	7.74%
Found:	81.48%	7.66%

Reference Example 15 (Raw material in Example 20)

(a)

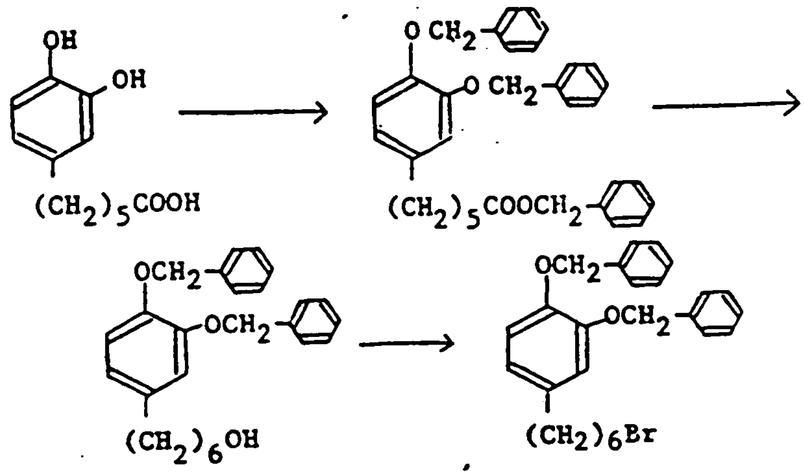


(60%)

A mixture of 2 g of oily sodium hydride/and 90 ml of dimethyl sulfoxide was stirred for 1 hour at 55-60°C and then allowed to cool to room temperature. To the mixture was added dropwise a mixture of 11 g of (4-carboxybutyl)triphenylphosphonium bromide and 25 ml of dimethyl sulfoxide at room temperature. Thereafter, the mixture was stirred for 30 minutes at room temperature

and then to the reaction mixture was added dropwise a mixture of 8 g of 3,4-dibenzyloxybenzaldehyde and 30 ml of dimethyl sulfoxide. After further stirring the mixture for one hour at room temperature, 5 g of dry ice was added to the reaction mixture and after further adding thereto 250 ml of water and 50 ml of an aqueous 10% hydrochloric acid solution, the product was extracted with 300 ml of ether. The extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced perssure to provide a sticky product. The product was applied to silica gel (150 ml) column chromatography and eluted with a mixture of n-hexane and ether (1 : 1) to provide 8.5 g of 6-(3,4-dibenzyloxyphenyl)-5-hexenoic acid. The product was dissolved in 30 ml of ethanol and catalytically reduced using 1 g of 10% palladium-carbon as a catalyst until the absorption of hydrogen stopped. Then, the catalyst was removed by filtration and the filtrate was concentrated under reduced pressure to provide 3.8 g of 6-(3,4-dihydroxyphenyl)hexanoic acid. Melting point 109°C.

(b)



A mixture of 3.8 g of 6-(3,4-dihydroxyphenyl)-hexanoic acid, 8.6 g of benzyl chloride, 9.4 g of potassium carbonate, 0.1 g of potassium iodide, 0.1 g of tetra-n-butylammonium bromide, and 50 ml of N,N-dimethylformamide was stirred overnight at room temperature. After the reaction was over, 200 ml of water was added to the reaction mixture and the product was extracted thrice each time with 100 ml of ether. The extracts were combined with each other, washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to provide a sticky product. The product was applied to silica gel (150 ml) column chromatography and eluted with a mixture of toluene and ethyl acetate (19 : 1) to provide 3.4 g of benzyl 6-(3,4-dibenzyloxyphenyl)-hexanate.

The product thus obtained was dissolved in 20 ml of ether and the solution was added dropwise to a mixture of 0.5 g of lithium aluminum hydride and 50 ml of ether under ice-cooling. Thereafter, the mixture was stirred

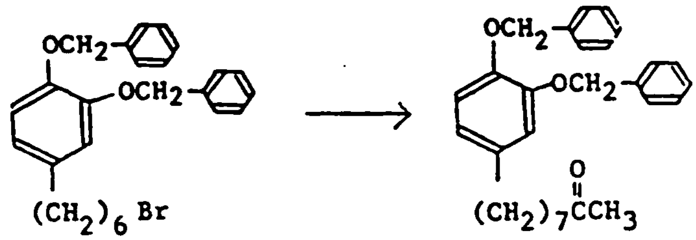
for one hour at room temperature and 30 ml of an aqueous 10% hydrochloric acid solution was added to the reaction mixture under ice-cooling. The organic layer thus formed was collected, washed with water, dried over anhydrous magnesium sulfate, and concentrated under reducced pressure to provide a sticky product. The product was applied to silica gel (100 ml) column chromatography and eluted with a mixture of toluene and ethyl acetate (4 : 1) to provide 1.95 g of 6-(3,4-dibenzyloxyphenyl)hexanol.

The product was dissolved in 10 ml of methylene chloride and the solution was added dropwise at room temperature to a methylene chloride solution (containing 0.45 g of pyridine) of triphenylphosphinedibromide prepared from 1.57 g of triphenylphosphine and 0.88 g of bromine. Thereafter, the mixture was stirred overnight at room temperature and the reaction mixture thus obtained was washed with diluted hydrochloric acid, washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was applied to silica gel (50 ml) column chromatography and eluted with a mixture of n-hexane and toluene (2 : 1) to provide 1.08 g of 6-(3,4-dibenzyloxyphenyl)hexyl bromide as an oil.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm)

1.0-2.0(8H), 2.50(2H), 3.38(2H), 5.13(2H), 5.16(2H), 6.6-6.92(3H), 7.10-7.60(10H).

(c)

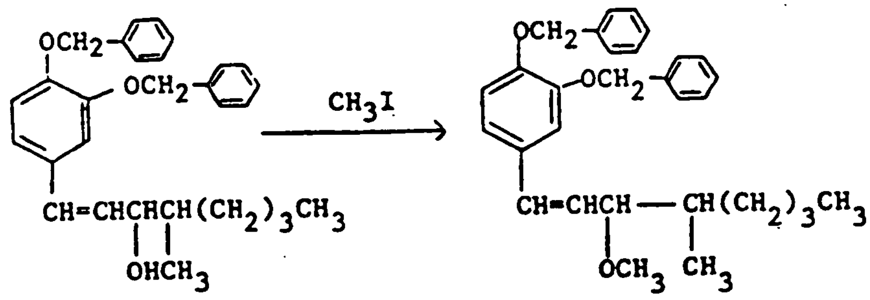


A mixture of 0.5 g of 6-(3,4-dibenzyloxyphenyl)-hexyl bromide , 0.12 g of acetylacetone, 0.15 g of potassium carbonate, 0.02 g of sodium iodide, and 5 ml of ethanol was refluxed for 20 hours. To the reaction mixture was added 15 ml of water and the product was extracted with 20 ml of ether. The extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to provide a sticky product. The product was applied to silica gel (45 ml) column chromatography and eluted with a mixture of toluene and ethyl acetate (30 : 1) to provide 33 mg of 9-(3,4-dibenzyloxyphenyl)-2-nonanone as an oil.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

1.0-2.0(10H), 2.10(3H), 2.20-2.70(4H), 3.08(2H), 3,10(2H), 6.50-7.0(3H), 7.20-7.60(10H).

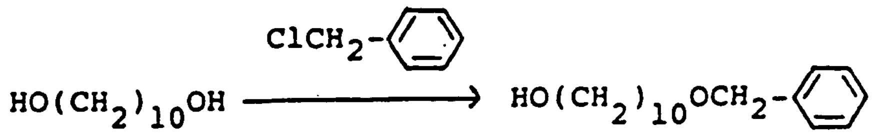
Reference Example 16



To a mixture of 130 mg of oily sodium hydride (60%) and 15 ml of N,N-dimethylformamide were added dropwise, in succession, a solution of 1.27 g of 1-(3,4-dibenzyloxyphenyl)-4-methyl-1-octen-3-ol obtained in Reference Example 1 in 5 ml of N,N-dimethylformamide and 500 mg of methyl iodide with stirring under ice-cooling. After stirring the mixture overnight at room temperature, 150 ml of water was added to the reaction mixture and the product was extracted with 30 ml of ethyl acetate. The extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to provide a sticky product. The product was applied to silica gel (40 g) column chromatography and eluted with a mixture of n-hexane and ether (4 : 1) to provide 970 mg of 1-(3,4-dibenzyloxyphenyl)-3-methoxy-4-methyl-1-octene. Melting point 36-38^{o}C.

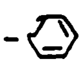
Reference Example 17 (Raw material in Example 23)

(a)

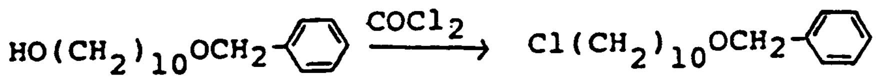


In 20 ml of xylene was dissolved 35 g of decanediol by heating and after adding thereto 1.65 g of metallic sodium at 130°C, the mixture was heated for one hour at 125 to 130°C. To the reaction mixture was added dropwise 9.5 g of benzyl chloride at 120-130°C and the mixture was further heated for one hour at 130°C. The reaction mixture was cooled to 110°C and after adding thereto 50 ml of toluene, the mixture was filtered while the mixture was in a hot state. The filtrate was ice-cooled to precipitate crystals, which were collected by filtration to recover 24 g of decanediol used as the raw material. On the other hand, the filtrate was concentrated under reduced pressure to provide an oily product. The product was applied to silica gel column chromatography and eluted with a mixture of toluene and ethyl acetate (8 : 2) to provide 13 g of oily 10-benzyloxy-1-decanol.

Nuclear magentic resonance spectra (in $CDCl_3$, TMS, ppm):

1.1-2.0(16H,$(CH_2)_8$), 3.43(2H, t, -$C\underline{H}_2$O-), 3.59(2H, t, -$C\underline{H}_2$-OH), 4.47(2H, s, -O$C\underline{H}_2$- ), 7.28(5H, H of benzene ring)

(b)

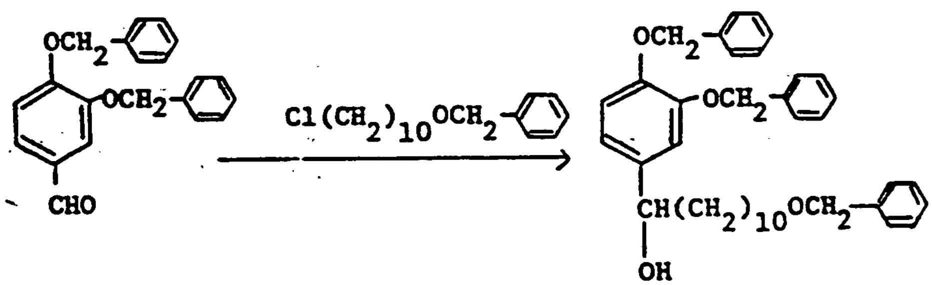


A mixture of 7 g of 10-benzyloxy-1-decanol, 8 ml of thionyl chloride, and 0.2 ml of dimethylformamide was heated to 50 to 60°C for one hour. After the reaction was over, the reaction mixture was concentrated under reduced pressure, the residue was dissolved in 50 ml of n-hexane, and after washing the solution with water, the solution was dried over anhydrous magnesium sulfate. Then, the solvent was distilled off and the residue was applied to silica gel column chromatography and eluted with toluene to provide 6.7 g of oily 10-benzyloxy-1-chlorodecane. Boiling point 135 - 140°C (0.6 - 0.9 mm Hg).

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS, ppm):

1.1-2.0(16H, $(CH_2)_8$), 3.43(2H, t, $-CH_2-O-$), 3.49(2H, t, $-CH_2Cl$), 4.47(2H, s, $-OCH_2-$), 7.28(5H, H of benzene ring).

(c)



To a mixture of 1 ml of anhydrous ether and 0.6 g of metallic magnesium were added 0.1 ml of ethyl iodide and a piece of iodine crystal followed by heating to initiate the reaction and then a mixture of 6.7 g of10-benzyloxy-1-chlorodecane and 10 ml of anhydrous ether was added dropwise to the aforesaid mixture. After the reaction was over, the reaction mixture was refluxed for 2 hours. After cooling, the reaction mixture was added dropwise to a solution of 6 g of 3,4-dibenzyloxybenzaldehyde dissolved in 30 ml of tetrahydrofuran at 0° to 5°C. Thereafter, the mixture was stirred for 30 minutes at room temperature and after adding 300 ml of an aqueous 1% hydrochloric acid solution to the reaction mixture, the product was extracted with 100 ml of toluene. The extract was washed with water, dried over anhydrous magnesium sulfate, and then the solvent was distilled off under reduced pressure. The residue was dissovled in 30 ml of ethanol, the solution was allowed to stand overnight under cooling to 0° to 5°C, and the crystals thus precipitated were collected by filtration. By drying the crystals, 5 g of 11-benzyloxy-1-(3,4-dibenzyloxyphenyl)-1-undecanol was obtained. Melting point 50 - 52°C.

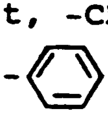
Elemental analysis for $C_{38}H_{46}O_4$:

	C	H
Calculated:	80.53%	8.18%
Found:	80.55%	7.94%

Reference Example 18 (Raw material in Example 24)

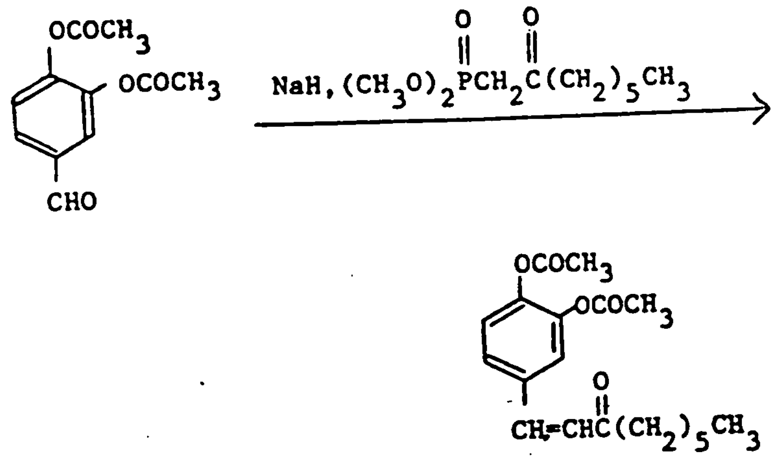
(a) To a mixture of 2.16 g of benzyl alcohol and 30 ml of dimethylformamide was added 1.2 g of oily sodium hydride (60%). After stirring the mixture for 30 minutes at 20° to $25^{\circ}C$, 10 g of 1,12-dibromododecane was added to the mixture in one portion followed by stirring for 2 hours at 25° to $30^{\circ}C$. After the reaction was over, 300 ml of water was added to the reaction mixture and the product was extracted with n-hexane. The extract was washed with water, dried over anhydrous magnesium sulfate, and then, the solvent was distilled off. The oily residue was applied to silica gel column chromatography and eluted with a mixture of n-hexane and ether (9 : 1) to provide 3.8 g of 12-benzyloxy-1-bromododecane as an oily product.

Nuclear magentic resonance spectra (in $CDCl_3$, TMS, ppm):

1.1-2.0(20H, $-(CH_2)_{10}-$), 3.38(2H, t, $-CH_2-Br$), 3,44(2H, t, $-CH_2-O-$), 4.47(2H, s, $-OCH_2-$ ), 7.28(5H, H of benzene ring)

(b) By follwoing the procedure as in Reference Example 17-(c) using the compound in the above step (a), the following compound was obtained.

Reference Example 21 (Raw material in Example 7)

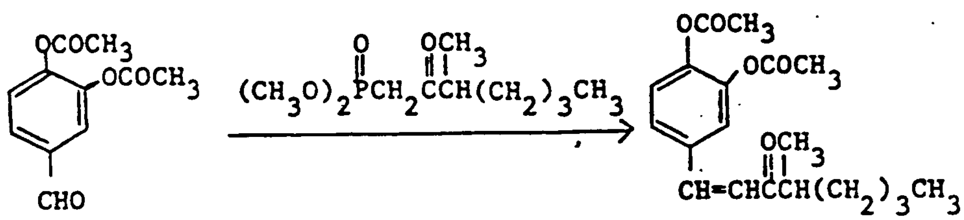


To a mixture of 400 mg of oily sodium hydride (60%) and 50 ml of 1,2-dimethoxyethane was added dropwise a mixture of 3.06 g of dimethyl 2-oxooctylphosphonate and 10 ml of dimethoxyethane with stirring under ice-cooling. After adding thereto 5 ml of dimethyl sulfoxide and stirring the mixture for one hour at room temperature, a mixture of 2.22 g of 3,4-diacetoxybenzaldehyde and 10 ml of dimethoxyethane was added dropwise to the mixture. After stirring the resultant mixture for 4 hours at room temperature, 400 ml of water was added to the reaction mixture and the product was extracted twice each time with 50ml of ether. The extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was applied to silica gel (120 g) column chromatography and eluted with a mixture of toluene and ethyl acetate (20 : 1) to provide 2.67 g of 1-(3,4-diacetoxyphenyl)-1-nonen-3-one.

Melting point 71 - 72°C.

By following the procedure as in Reference Example 21, the compounds of following Reference Examples 22 to 24 were prepared.

Reference Example 22 (Raw material in Example 28)



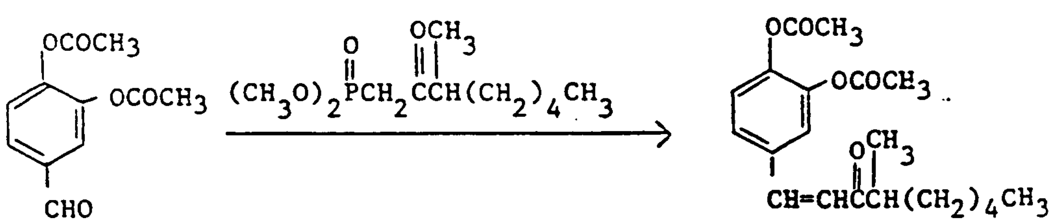
1-(3,4-Diacetoxyphenyl)-4-methyl-1-octen-3-one.

Oily product.

Nuclear magnetic resonance spectra (In $CDCl_3$, TMS internal standard, ppm):

0.89(3H), 1.05-1.9(9H), 2.30(6H), 2,75(1H), 6.6-7.7(5H).

Reference Example 23 (Raw material in Example 29)



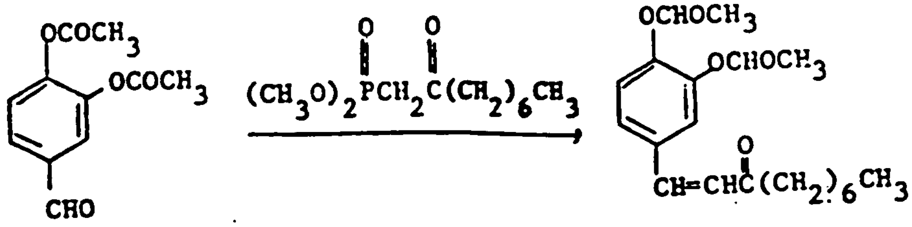
1-(3,4-Diacetoxyphenyl)-4-methyl-1-nonen-3-one.

Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.88(3H), 1.05-1.9(11H), 2.30(6H), 2.77(1H), 6.66-7.7(5H).

Reference Example 24 (Raw material in Example 30)



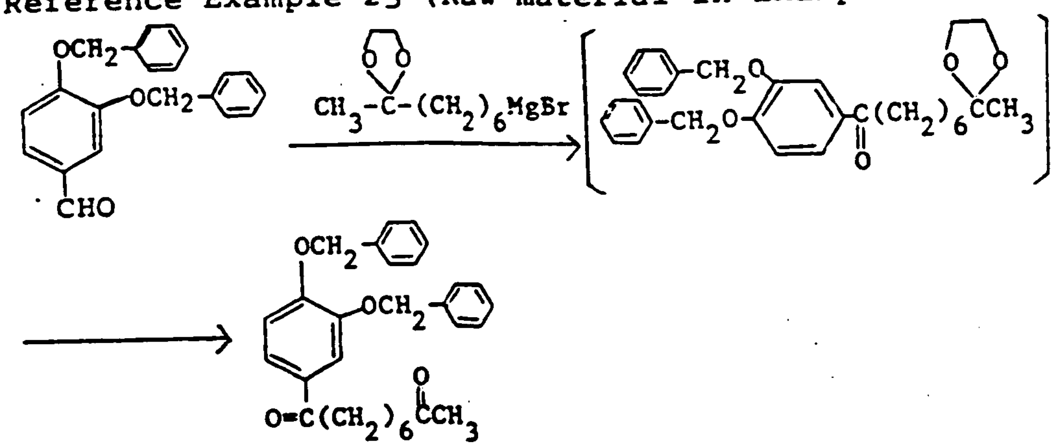
1-(3,4-Diacetoxyphenyl)-1-decen-3-one.

Melting point 66 - 67°C.

Elemental analysis for $C_{20}H_{26}O_5$:

	C	H
Calculated:	69.34%	7.56%
Found:	69.33%	7.72%

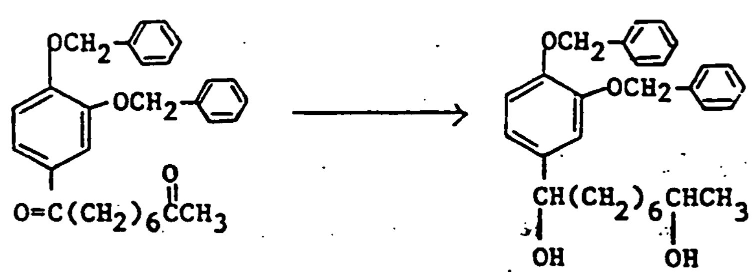
Reference Example 25 (Raw material in Example 31)



To a mixture of 12.7 g of 3,4-dibenzyloxybenzaldehyde and 150 ml of tetrahydrofuran was added dropwise an ether solution of Grignard reagent prepared from 10.4 g of 2-methyl-2-(6-bromohexyl)-1,3-dioxolane and 1.1 g of magnesium at a temperature below 5°C. After stirring the mixture for 2 hours at room temperature, water was added to the mixture and acidifying the mixture by the addition of

diluted hydrochloric acid, the reaction mixture thus obtained was extracted with toluene. The extract was washed with water, dried by anhydrous magnesium sulfate, and concentrated under reduced pressure. To the residue were added 300 ml of acetone and 0.1 g of p-toluenesulfonic acid, the mixture was stirred overnight at room temperature and concentrated under reduced pressure. The residue was extracted with toluene and the extract was washed with an aqueous 5% sodium hydrogencarbonate solution, washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to provide an oily product. The product was applied to silica gel (500 ml) column chromatography and eluted with a mixture of toluene and ethyl acetate (19 : 1) to provide 4.4 g of 1-(3,4-dibenzyloxyphenyl)-1,8-nonanedione. Melting point 64 - 66°C.

Reference Example 26 (Raw material in Example 32)



A mixture of 0.8 g of 1-(3,4-dibenzyloxyphenyl)-1,8-nonanedione and 10 ml of tetrahydrofuran was added to a solution of 0.1 g of lithium aluminum hydride in 50 ml of ether under ice-cooling followed by stirring

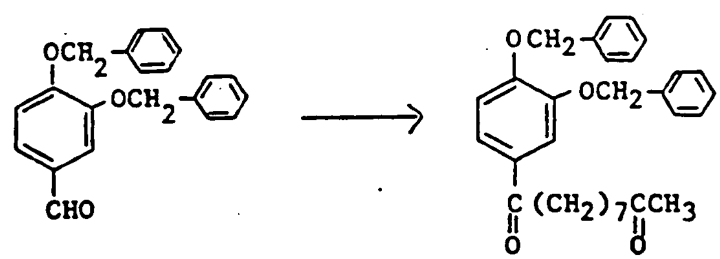
for 2 hours at room temperature. Then, 50 ml of toluene was added to the reaction mixture and the mixture was acidified by the addition of diluted hydrochloric acid. The toluene layer was collected, washed with an aqueous 5% sodium hydrogencarbonate solution, washed with water, dried over anhydrous magnesium carbonate, and concentrated under reduced pressure to provide 0.8 g of 1-(3,4-dibenzyloxyphenyl)-1,8-nonanediol as an oil.

Nuclear magentic resonance spectra (in $CDCl_3$, TMS, ppm):

1.05-1.80(15H), 3.8-4.0(1H), 4.56(1H), 5.18(2H), 5.20(2H), 6.80-7.60(13H).

Reference Example 27 (Raw material in Example 33)

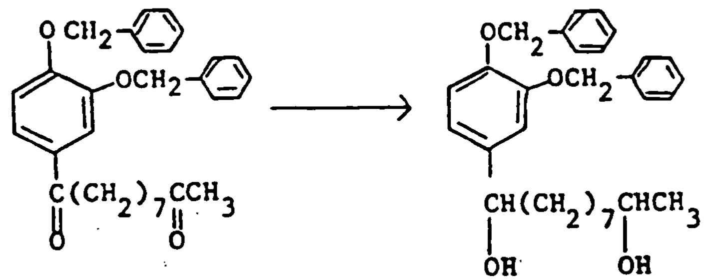
(a)



By following the procedure as in Reference Example 25 using a Grignard reagent prepared from 3 g of 3,4-dibenzyloxybenzaldehyde, 2.5 g of 2-methyl-(7-bromo-heptyl)-1,3-dioxolane, and 0.3 g of magnesium, 0.8 g of 1-(3,4-dibenzyloxyphenyl)-1,9-decanedione was obtained.

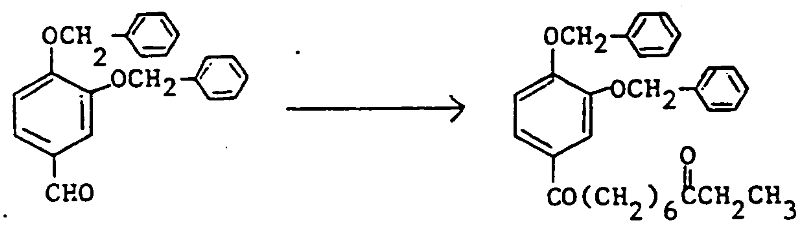
Melting point 72 - 74°C.

(b)



By following the procedure as in Reference Example 26 using 1 g of 1-(3,4-dibenzyloxyphenyl)-1,9-decanedione as the raw material, 1.0 g of 1-(3,4-dibenzyloxyphenyl)-1,9-decanediol was obtained. Melting point 66°C.

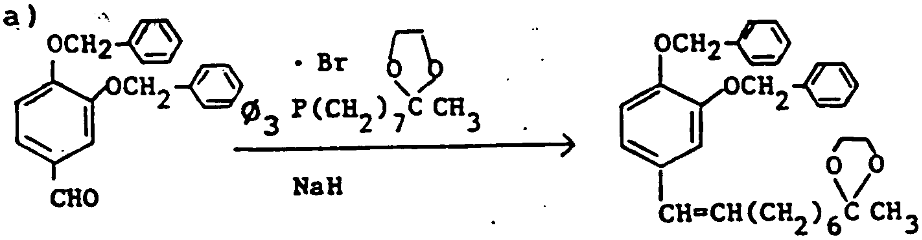
Reference Example 28 (Raw material in Example 34)



By follwoing the procedure as in Reference Example 25 using 8 g of 3,4-dibenzyloxybenzaldehyde, and a Grignard reagent prepared from 8 g of 2-ethyl-2-(6-bromohexyl)-1,3-dioxsolane, and 850 mg of magnesium, 2 g of 1-(3,4-dibenzyloxyphenyl)-1,8-decanedione was obtained. Melting point 67 - 68°C.

Reference Example 29 (Raw material in Example 35)

(a)

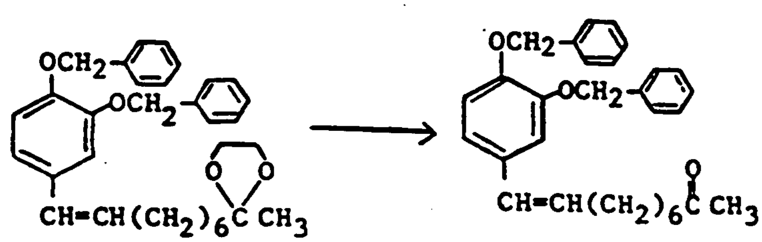


A mixture of 640 mg of oily sodium hydride (60%) and 10 ml of dimethyl sulfoxide was stirred for 45 minutes at 75 to 80°C. After cooling the mixture, a mixture of 50 ml of dimethyl sulfoxide and 8.2 g of 8-ethylenedioxynonyl triphenylphosphonium bromide prepared from 2-methyl-2-(7-bromoheptyl)-1,3-dioxolan and triphenylphosphin was added to the mixture. After 10 minutes, a mixture of 2.5 g of 3.4-dibenzyloxybenzaldehyde and 10 ml of diemthyl sulfoxide was added to the mixture at room temperature and the resultant mixture was stirred overnight. To the reaction mixture was added 500 ml of water and the product was extracted with ether. The extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to provide an oily product. The product was applied to silica gel (200 ml) column chromatography and eluted with a mixture of n-hexane and ether (1 : 1) to provide 1.4 g of 1-(3,4-dibenzyloxyphenyl)-9-ethylenedioxy-1-decene.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS, ppm):

1.05-1.8(11H), 1.9-2.4(2H), 3.85(4H), 5.05(4H), 6.0-7.5(15H).

(b)

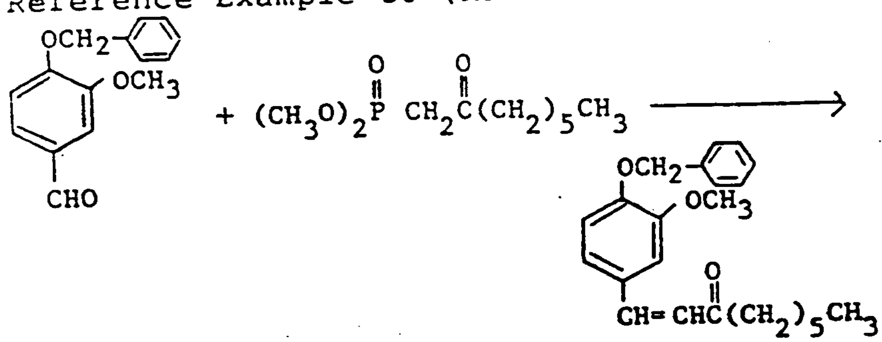


A mixture of 1.4 g of 1-(3,4-dibenzyloxyphenyl)-9-ethylenedioxy-1-decene, 50 ml of acetone, and 50 mg of p-toluenesulfonic acid was stirred overnight at room temperature. After adding thereto 50 mg of sodium carbonate, the reaction mixture was concentrated under reduced perssure, and after adding thereto 50 ml of water, the product was extracted with toluene. The extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to provide 1.1 g of 1-(3,4-dibenzyloxyphenyl)-1-decen-9-one as an oil.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS, ppm):

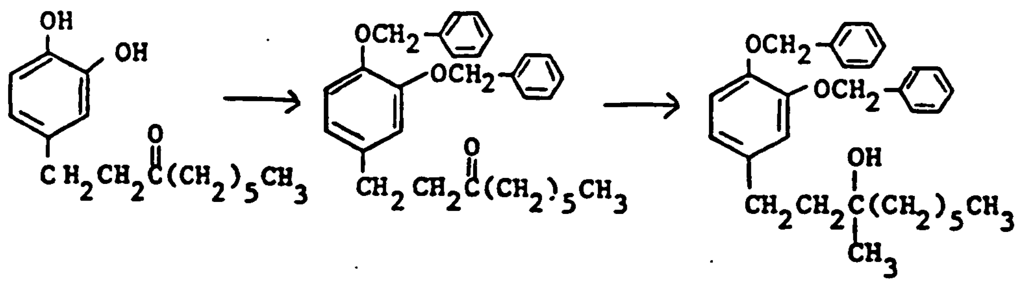
1.05-1.8(8H), 2.1(3H), 2.1-2.6(4H), 5.16(4H), 6.0-7.6(15H).

Reference Example 30 (Raw material in Example 36)



By following the procedure as in Reference Example 1 (a) using 1.2 g of 4-benzyloxy-3-methoxybenzaldehyde and 1.53 g of dimethyl 2-oxooctylphosphonate, 1.27 g of 1-(4-benzyloxy-3-methoxyphenyl)-1-nonen-3-one was obtained. Melting point 78 - 81°C.

Reference Example 31 (Raw material in Example 37)



(a) To a solution of 1.2 g of 1-(3,4-dihydroxyphenyl)-3-nonanone in 10 ml of dimethylformamide was added 200 mg of oily sodium hydride (60%) and after stirring the mixture for 15 minutes at room temperature, 0.9 g of benzyl bromide was added to the mixture followed by stirring for 15 minutes at room temperature. After further adding thereto 200 mg of oily sodium hydride (60%) and stirring the mixture for 15 minutes at room temperature, 0.9 g of benzyl bromide was added to the mixture followed by stirring for 1.5 hours at room temperature. After adding 50 ml of water to the reaction mixture, the product was extracted with toluene. The extract was washed with water, dried over anhydrous magnesium sulfate, and then the solvent was distilled off under reduced pressure. The residue was applied to silica gel column chromatography and eluted with toluene to provide 1.8 g of 1-(3,4-dibenzyloxyphenyl)-3-nonanone as a sticky product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS, ppm):

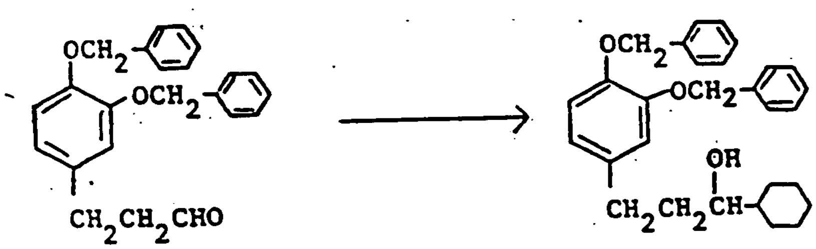
0.87(3H, $-CH_3$), 1.05-1.8(8H, $-(CH_2)_4-$), 1.30(2H, $-CH_2-$), 2.55-2.85(4H, $-CH_2\overset{O}{\overset{\|}{C}}CH_2-$), 5.07(4H, $-OCH_2$ x 2), 6.5-7.5(13H)

(b) A solution of 1.75 g of 1-(3,4-dibenzyloxyphenyl)-3-nonanone in 10 ml of tetrahydrofuran was cooled to 0° to 5°C and then an ether solution of a Grignard reagent prepared from 0.24 g of metallic magnesium and 1.7 g of methyl iodide was added dropwise to the mixture. Thereafter, the resultant mixture was stirred for 15 minutes and after adding thereto 50 ml of an aqueous 5% hydrochloric acid solution, the product was extracted with toluene. The extract was washed with water, dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressure to provide 1.6 g of 1-(3,4-dibenzyloxyphenyl)-3-methyl-3-nonanol.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS, ppm):

0.88(3H, $-CH_3$), 1.1-1.9(15H, $-\underline{CH_2}-\overset{CH_3}{\overset{|}{C}}(OH)-(CH_2)_5-$, [1.18(3H, $-CH_3$)]), 2.4-2.8(2H, $-CH_2-$), 5.08(4H, $-OCH_2-$ x 2), 6.5-7.6(13H).

Reference Example 32 (Raw material in Example 38)

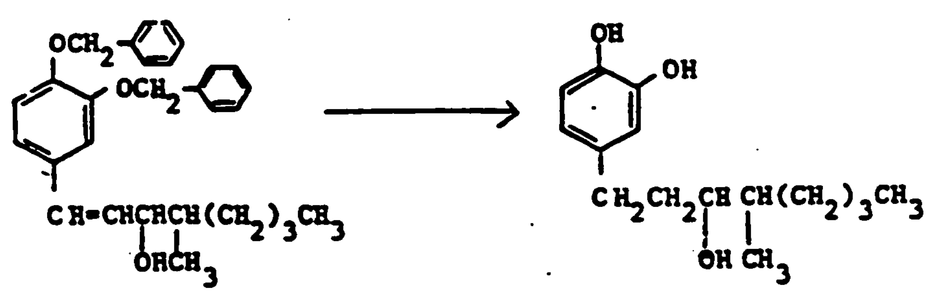


A solution of 0.4 g of 3-(3,4-dibenzyloxyphenyl)-propionaldehyde in 5 ml of anhydrous tetrahydrofuran was cooled to 0° to 5°C and then 5 ml of an ether solution of cyclohexyl magnesium bromide prepared from 0.12 g of metallic magnesium and 0.82 g of cyclohexyl bromide was added dropwise to the solvent. Thereafter, the reaction mixture was stirred for 15 minutes and after adding thereto 50 ml of an aqueous 5% hydrochloric acid solution, the product was extracted with 30 ml of toluene. The extract was washed with water, dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressure to provide an oily product. The product was applied to silica gel column chromatography and eluted with toluene to provide 0.2 g of 3-(3,4-dibenzyloxyphenyl)-1-cyclohexyl-1-propanol. Melting point 107 - 108°C.

Elemental analysis for $C_{29}H_{30}O_3$:

	C	H
Calculated:	80.89%	7.96%
Found:	80.88%	8.15%

Example 1



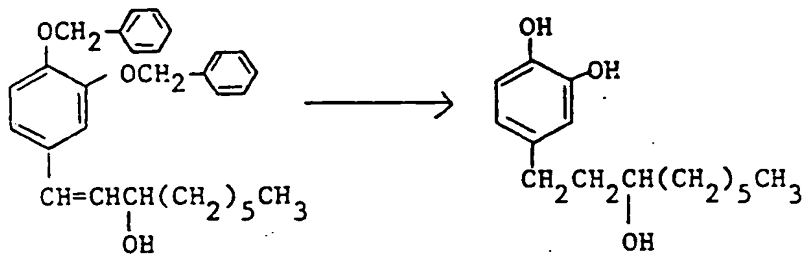
In 20 ml of ethanol was dissolved 0.4 g of 1-(3,4-

dibenzyloxyphenyl)-4-methyl-1-octen-3-ol and the compound thus dissolved was catalytically reduced using 0.1 g of 10% palladium-carbon as a catalyst until the absorption of hydrogen stopped. After the reaction was over, the catalyst was filtered off and the filtrate was concentrated under reduced pressure to provide 0.23 g of 1-(3,4-dihdyroxyphenyl)-4-methyl-3-octanol.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.7-1.8(15H), 2.57(2H), 3.45(1H), 6.4-6.8(3H)

Example 2

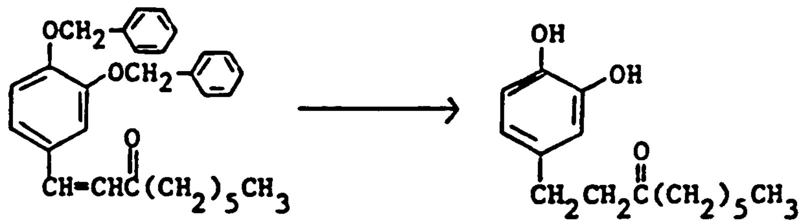


By following the same procedure as in Example 1 using 0.85 g of 1-(3,4-dibenzyloxyphenyl)-1-nonen-3-ol, 0.4 g of 1-(3,4-dihydroxyphenyl)-3-nonanol was obtained.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.8-1.9(15H), 2.55(2H), 3.60(1H), 6.4-6.8(3H)

Example 3



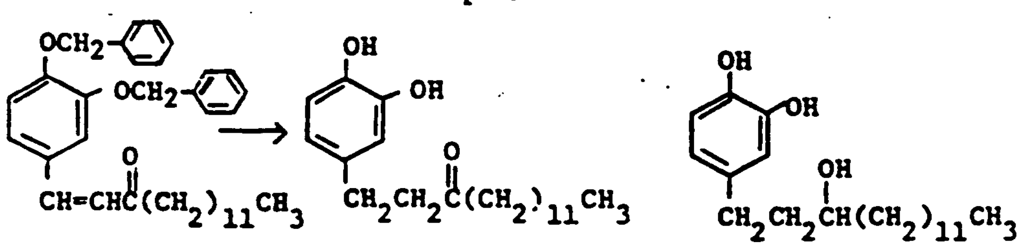
Using 0.2 g of 10% palladium-carbon as catalyst, 0.5 g of 1-(3,4-dibenzyloxyphenyl)-1-nonen-3-one was catalytically reduced in a mixture of 10 ml of methanol and 10 ml of ethyl acetate until the absorption of hydrogen stopped. Then, the catalyst was filtered off and the filtrate was concentrated under reduced pressure. The residue was applied to silica gel column chromatography and eluted with a mixture of toluene and ethyl acetate (10 : 1) to provide 0.2 g of white crystals of 1-(3,4-dihydroxyphenyl)-3-nonanone.

Melting point 50 - 53°C.

Elemental analysis for $C_{15}H_{22}O_3$:

	C	H
Calculated:	71.97%	8.86%
Found:	71.66%	8.77%

Example 4



(a) (b)

In a mixture of 30 ml of ethyl acetate and 5 ml of ethanol was dissolved 1.5 g of 1-(3,4-dibenzyloxyphenyl)-1-pentadecen-3-one and the compound was catalytically reduced using 0.2 g of 10% palladium-carbon as a catalyst until the absorption of hydrogen stopped. Then, the catalyst was filtered off and the filtrate was concentrated under reduced pressure. The residue was applied to silica gel (80 ml) column chromatography and eluted with a mixture of toluene and ethyl acetate (10 : 1) to provide 0.55 g of white crystals of 1-(3,4-dihydroxyphenyl)-3-pentadecanone (a) as the eluate first merging from the column. Melting point 67 - 68°C.

Elemental analysis for $C_{21}H_{34}O_3$:

	C	H
Calculated:	75.41%	10.24%
Found:	75.12%	10.38%

After the elution of 1-(3,4-dihydroxyphenyl)-3-pentadecanone was over, further elution was carried out with toluene to provide 0.1 g of 1-(3,4-dihydroxyphenyl)-3-pentadecanol (b) as a white crystals.

Melting point 63 - 64°C.

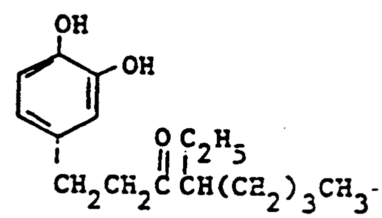
Elemental analysis for $C_{21}H_{36}O_3$:

	C	H
Calculated:	74.95%	10.78%
Found:	74.88%	10.81%

By following the procedure as in Example 4, the compounds in following Examples 5 to 8 were prepared.

Example 5

(Using the compound obtained in Reference Example 4)



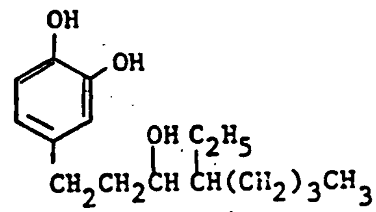
(a)

1-(3,4-Dihydroxyphenyl)-4-ethyl-3-octanone (a).

Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.6-1.8(14H), 2.3(1H), 2.67(4H), 6.4-6.8(3H)

(b) 

1-(3,4-Dihydroxyphenyl)-4-ethyl-3-octanol (b).

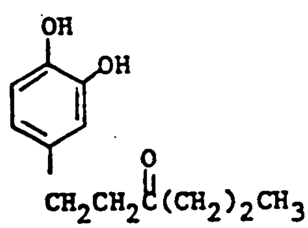
Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.85(6H), 1.1-1.9(11H), 2.67(2H), 3.63(1H), 6.4-6.7(3H).

Example 6

(Using the compound obtained in Reference Example 5)

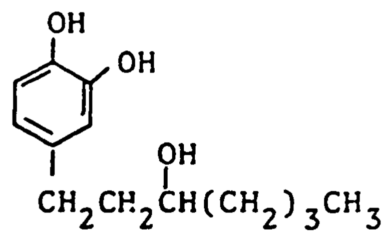
(a) 

1-(3,4-Dihydroxyphenyl)-3-hexanone (a).

Melting point 37 - 39°C.

Elemental analysis for $C_{12}H_{16}O_3$:

	C	H
Calculated:	69.21%	7.74%
Found:	68.94%	7.91%



(b)

1-(3,4-Dihydroxyphenyl)-3-hexanol (b).

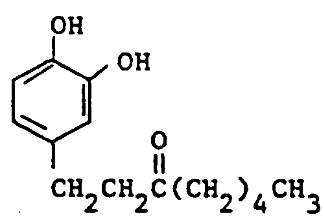
Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.9(3H), 1.1-1.9(6H), 2.6(2H), 3.65(1H), 6.6-6.9(3H).

Example 7

(Using the compound obtained in Reference Example 6)



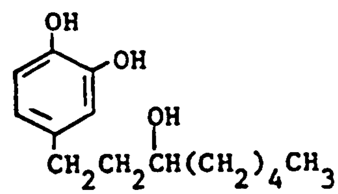
(a)

1-(3,4-Dihydroxyphenyl)-3-octanone (a).

Melting point 53 - 55°C.

Elemental analysis for $C_{14}H_{20}O_3$:

	C	H
Calculated:	71.16%	8.53%
Found:	70.87%	8.74%



(b)

1-(3,4-Dihydroxyphenyl)-3-octanol (b).

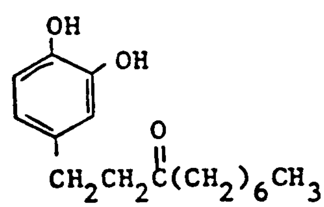
Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.9(3H), 1.1-1.9(10H), 2.6(2H), 3.65(1H), 6.5-6.9(3H).

Example 8

(Using the compound obtained in Reference Example 7)



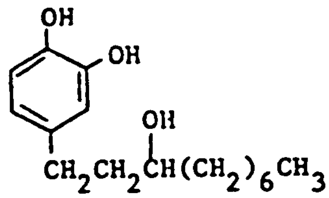
(a)

1-(3,4-Dihydroxyphenyl)-3-decanone (a)

Melting point 65 - 66°C.

Elemental analysis for $C_{16}H_{24}O_3$:

	C	H
Calculated:	72.69%	9.15%
Found:	72.42%	9.48%



(b)

1-(3,4-Dihydroxyphenyl)-3-decanol (b).

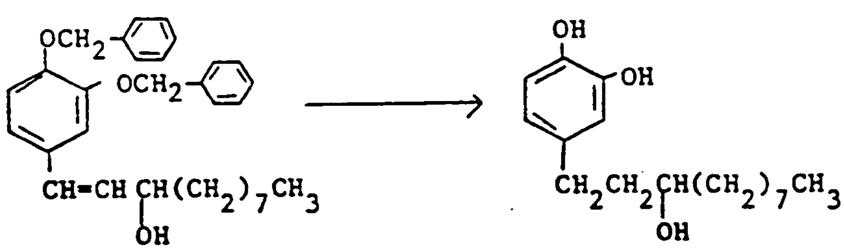
Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.9(3H), 1.1-1.9(14H), 2.6(2H), 3.65(1H), 6.5-6.9(3H).

By following the procedure as in Example 1, the compounds of following Examples 9 to 11 were prepared.

Example 9



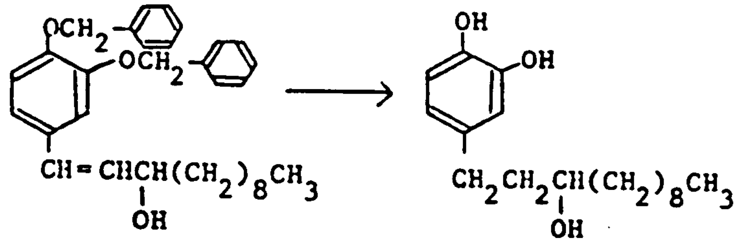
1-(3,4-Dihydroxyphenyl)-3-undecanol .

Melting point 45 - 47°C.

Elemental analysis for $C_{17}H_{28}O_3$:

	C	H
Calculated:	72.82%	10.06%
Found:	72.76%	10.29%

Example 10



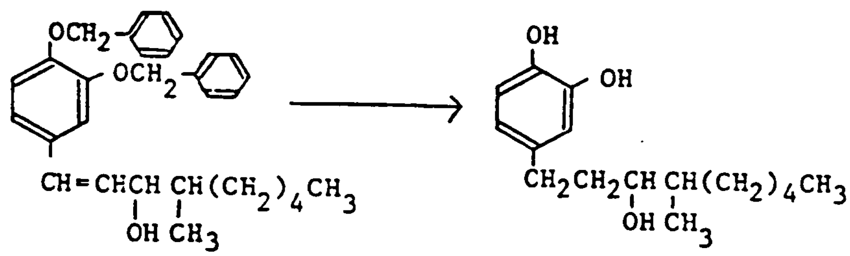
1-(3,4-Dihydroxyphenyl)-3-dodecanol.

Melting point 53 - 55°C.

Elemental analysis for $C_{18}H_{30}O_3$:

	C	H
Calculated:	73.43%	10.27%
Found:	73.48%	10.47%

Example 11



1-(3,4-Dihydroxyphenyl)-4-methyl-3-nonanol.

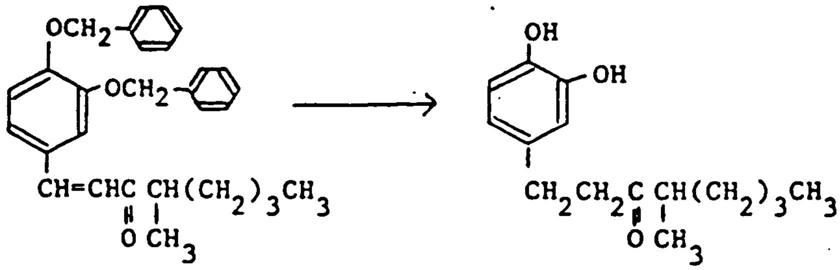
Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.7-1.9(17H), 2.58(2H), 3.55(1H), 6.5-6.9(3H),

By following the same procedure as in Example 3, the compound of following Example 12 was prepared.

Example 12



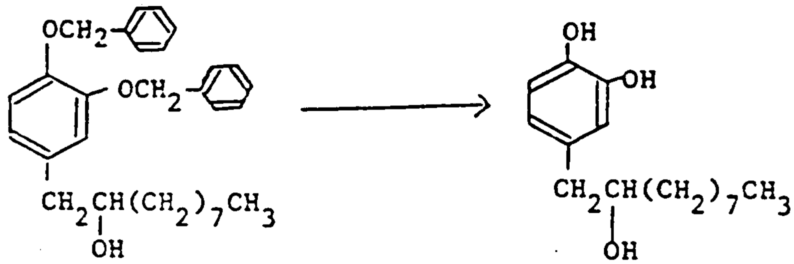
1-(3,4-Dihydroxyphenyl)-4-methyl-3-octanone.

Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard. ppm):

0.6-1.8(12H), 2.5(1H), 2.74(4H), 6.4-6.8(3H)

Example 13



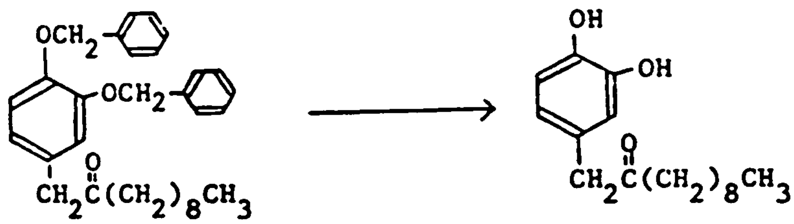
In 10 ml of ethanol was dissolved 0.5 g of 1-(3,4-dibenzyloxyphenyl)-2-decanol and the compound was catalytically reduced using 0.2 g of 10% palladium-carbon at room temperature and under atomospheric until the absorption of hydrogen stopped. After the reaction was over, the catalyst was filtered off and the filtrate was concentrated under reduced pressure to provide 0.28 g of 1-(3,4-dihydroxyphenyl)-2-decanol . Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.89(3H, $-CH_3$), 1.1-1.7(14H, $-(CH_2)_7-$), 1.62 (2H, $-CH_2-$), 3.74(1H, $-\underline{CH}(OH)-$), 6.4-6.9(3H, H of benzene

ring)

Example 14

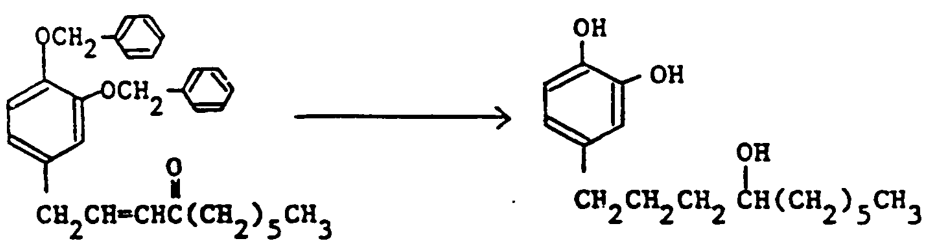


By following the same procedure as in Example 13 using 0.3 g of 1-(3,4-dibenzyloxyphenyl)-2-undecanone, 140 mg of 1-(3,4-dihydroxyphenyl)-2-undecanone was obtained. Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.86(3H, $-CH_3$), 1.0-1.7(14H, $-(CH_2)_7-$), 2.47(2H, $-CH_2-$), 3.56(2H, $-CH_2-$), 6.6-6.9(3H, H of benzene ring)

Example 15



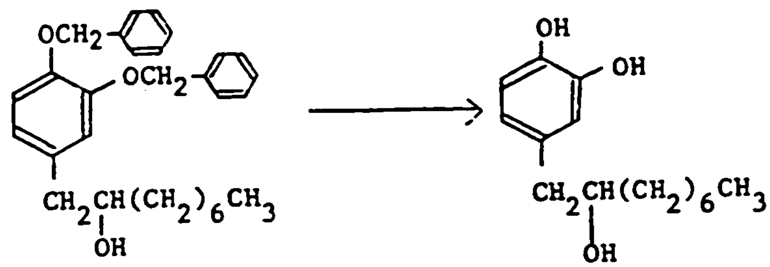
By following the same procedure as in Example 4 using 0.3 g of 1-(3,4-dibenzyloxyphenyl)-2-decen-4-one, 0.1 g of 1-(3,4-dihydroxyphenyl)-4-decanol was obtained. Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.86(3H, $-CH_3$), 1.1-1.8(14H), 1.48(2H, $-CH_2-$),

3.61(1H, $\overset{\text{OH}}{-\text{C}\underline{\text{H}}-}$), 6.4-6.8(3H, H of benzene ring).

Example 16

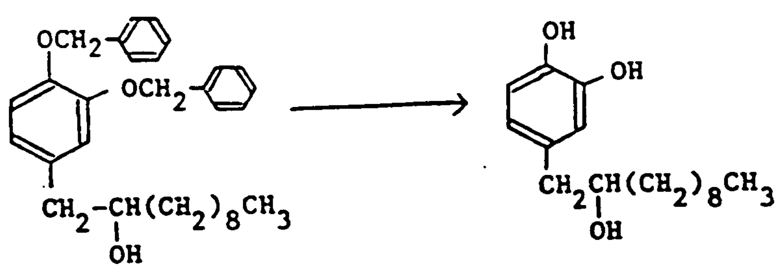


By following the same procedure as in Example 13 using 0.5 g of 1-(3,4-dibenzyloxyphenyl)-2-nonanol, 0.27 g of 1-(3,4-dihydroxyphenyl)-2-nonanol was obtained. Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.89(3H, $-CH_3$), 1.1-1.7(12H, $-(CH_2)_6-$), 1.62(2H, $-CH_2-$), 3.75(1H, $-C\underline{H}(OH)-$), 6.4-6.9(3H, H of benzene ring).

Example 17

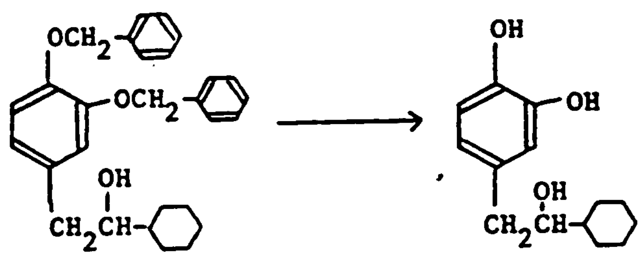


By following the same procedure as in Example 13 using 0.5 g of 1-(3,4-dibenzyloxyphenyl)-2-undecanol, 0.29 g of 1-(3,4-dihydroxyphenyl)-2-undecanol was obtained. Melting point 56 - 58°C.

Elemental analysis for $C_{17}H_{28}O_3$:

	C	H
Calculated:	72.82%	10.06%
Found:	72.70%	10.26%

Example 18

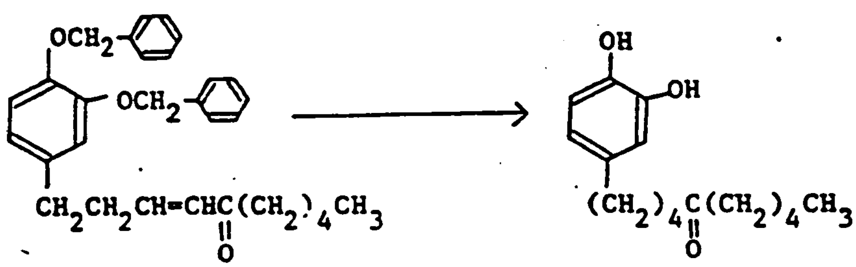


By following the same procedure as in Example 13 using 0.15 g of 2-(3,4-dibenzyloxyphenyl)-1-cyclohexyl-1-ethanol, 0.06 g of 2-(3,4-dihdyroxyphenyl)-1-cyclohexyl-1-ethanol was obtained. Melting point 106 - 108°C.

Elemental analysis for $C_{14}H_{20}O_3$:

	C	H
Calculated:	71.16%	8.53%
Found:	70.99%	8.61%

Example 19



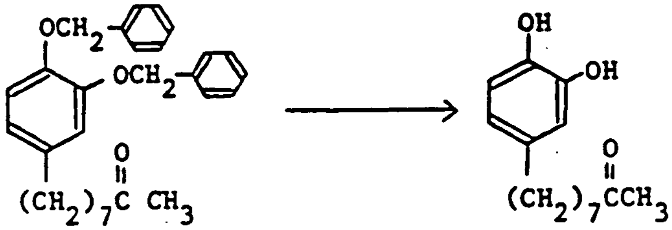
By following the same procedure as in Example 4 using 0.54 g of 1-(3,4-dibenzyloxyphenyl)-3-decen-5-one, 0.28 g of 1-(3,4-dihydroxyphenyl)-5-decanone was

obtained. Melting point 76 - 78°C.

Elemental analysis for $C_{16}H_{24}O_3$:

	C	H
Calculated:	72.14%	9.84%
Found:	72.18%	9.75%

Example 20

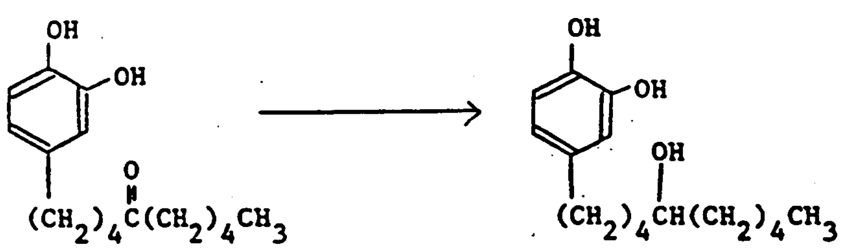


By following the same procedure as in Example 13 using 0.3 g of 9-(3,4-dibenzyloxyphenyl)-2-nonanone, 0.16 g of 9-(3,4-dihydroxyphenyl)-2-nonanone was obtained. Oily product.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

1.0-1.80(10H), 2.16(3H), 2.30-2.60(4H), 6.50-6.90(3H).

Example 21



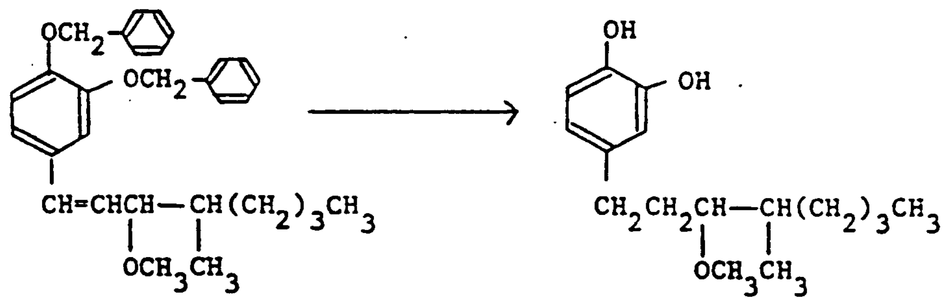
In 1.5 ml of methanol was dissolved 150 mg of 1-(3,4-dihydroxyphenyl)-5-decanone and 20 mg of sodium borohydride was added to the solution under ice-cooling followed by stirring for 30 minutes. Then, the solvent

was distilled off from the reaction mixture and after adding 10 ml of water to the residue thus formed, the product was extracted with ether. The extract was dried over anhydrous magnesium sulfate and the solvent was distilled off to provide white crystals of 1-(3,4-dihydroxyphenyl)-5-decanol, which was collected by filtration with the addition of n-hexane. Yield 117mg.

Elemental analysis for $C_{16}H_{26}O_3$:

	C	H
Calculated:	72.14%	9.84%
Found:	72.18%	9.75%

Example 22



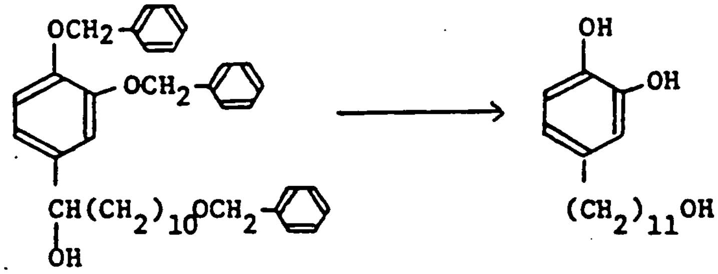
Using 0.1 g of 10% palladium-carbon as catalyst, 560 mg of 1-(3,4-dibenzyloxyphenyl)-3-methoxy-4-methyl-1-octene was catalytically reduced in a mixture of 5 ml of methanol and 5 ml of ethyl acetate until the absorption of hydrogen stopped. Thereafter, the catalyst was filtered off and the filtrate was concentrated under reduced perssure to provide 330 mg of oily 1-(3,4-dihydroxyphenyl)-3-methoxy-4-methyl-octane.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS

internal standard, ppm):

0.7-1.9(5H), 2.52(2H), 3.05(1H), 3.40(3H), 6.5-6.9(3H).

Example 23



In 40 ml of acetic acid was dissolved 4.4 g of 11-benzyloxy-1-(3,4-dibenzyloxyphenyl)-1-undecanol and the compound was catalytically reduced in the presence of 1 g of 10% palladium-carbon at room temperature and under atomospheric pressure until the absorption of hydrogen stopped. After the reaction was over, the catalyst was filtered off and after adding 300 ml of water to the filtrate, the product was extracted twice each time with 70 ml of ethyl acetate. The extract was washed with water, dried over anhydrous magnesium sulfate, and then the solvent was distilled off to provide a solid product. The solid product was recrystallized from 10 ml of a mixture of ethyl acetate and toluene (1 : 1) to provide 1.5 g of 11-(3,4-dihydroxyphenyl)-1-undecanol.

Melting point 92 - 93°C.

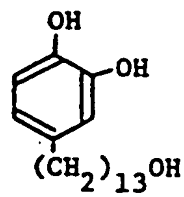
Elemental analysis for $C_{17}H_{28}O_3$:

	C	H
Calculated:	72.82%	10.06%
Found:	73.06%	10.29%

By following the procedure as in Example 23, the compounds of following Examples 24 and 25 A, B were perpared.

Example 24

(Using the compound obtained in Reference Example 18 step (b))



13-(3,4-Dihydroxyphenyl)-1-tridecanol

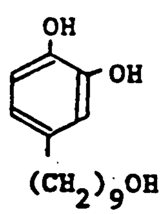
Melting point 93 - 95°C.

Elemental analysis for $C_{19}H_{32}O_3$:

	C	H
Calculated:	73.98%	10.46%
Found:	73.73%	10.75%

Example 25 A

(Using the compound obtained in Reference Example 19 A step (b))



9-(3,4-Dihydroxyphenyl)-1-nonanol

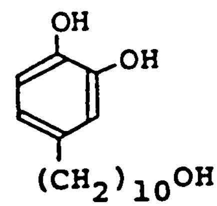
Melting point 89 - 91°C.

Elemental analysis for $C_{15}H_{24}O_3$:

	C	H
Calculated:	71.39%	9.59%
Found:	71.12%	9.80%

Example 25 B

(Using the compound obtained in Reference Example 19 B step (b))



10-(3,4-Dihydroxyphenyl)-1-decanol.

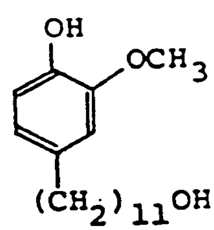
Melting point 89 - 91°C.

Elemental analysis for $C_{16}H_{26}O_3$:

	C	H
Calculated:	72.14%	9.84%
Found:	71.96%	10.11%

Example 26

(Using the compound obtained in Reference Example 20)

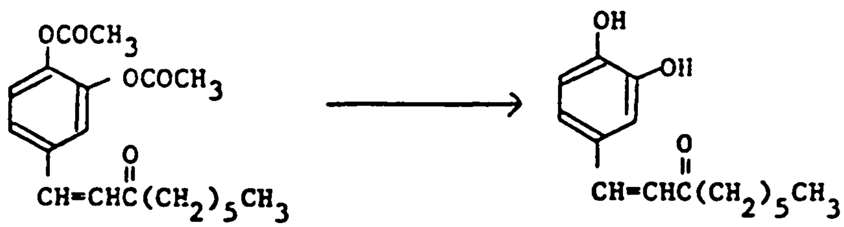


By following the procedure as in Example 23, 11-(4-hydroxy-3-methoxyphenyl)-1-undecanol was obtained. Melting point 72 - 74°C.

Elemental analysis for $C_{18}H_{30}O_3$:

	C	H
Calculated:	73.33%	10.27%
Found:	73.09%	10.26%

Example 27

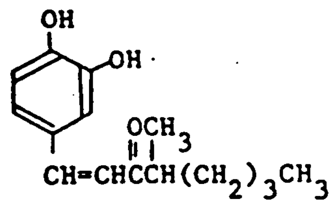


In 10 ml of methanol was dissolved 830 mg of 1-(3,4-diacetoxyphenyl)-1-nonen-3-one and after adding 7.5 ml of an aqueous 1 N-sodium hydroxide solution to the solution, the mixture was stirred for 30 minutes at room temperature. Then, the reaction mixture was ice-cooled and after adding thereto 25 ml of water, the mixture was acidified with the addition of 5 ml of an aqueous 1N-hydrochloric acid solution to form crystals, which were collected by filtration and washed with water to provide 580 mg of 1-(3,4-dihydroxyphenyl)-1-nonen-3-one. Melting point 114 - 115°C.

Elemental analysis for $C_{15}H_{20}O_3$:

	C	H
Calculated:	72.55%	8.12%
Found:	72.32%	8.23%

Example 28

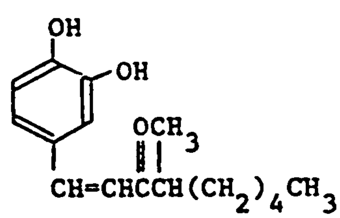


A hydrochloric acid-acidified aqueous solution obtained by following the same procedure as in Example 27 using 1.0 g of 1-(3,4-diacetoxyphenyl)-4-methyl-1-octen-3-one, was extracted twice each time with 20 ml of ether. The extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced perssuer to provide 0.7 g of oily 1-(3,4-dihydroxyphenyl)-4-methyl-1-octen-3-one.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standard, ppm):

0.88(3H), 1.05-1.9(9H), 2.85(1H), 6.59-7.7(5H)

Example 29

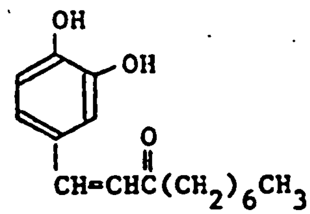


By following the same procedure as in Example 28 using 1.0 g of 1-(3,4-diacetoxyphenyl)-4-methyl-1-nonen-3-one, 0.7 g of 1-(3,4-dihydroxyphenyl)-4-methyl-1-nonen-3-one was obtained as an oil.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS internal standatd, ppm):

0.88(3H), 1.05-1.9(11H), 2.84(1H), 6.59-7.7(5H)

Example 30

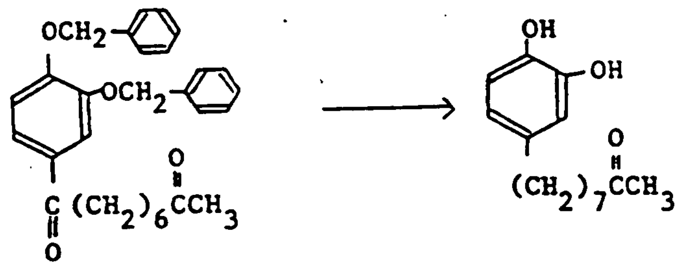


By following the same procedure as in Example 27 using 0.25 g of 1-(3,4-diacetoxyphenyl)-1-decen-3-one, 0.14 g of 1-(3,4-dihydroxyphenyl)-1-decen-one was obtained. Melting point 116 - 118°C.

Elemental analysis for $C_{16}H_{22}O_3$:

	C	H
Calculated:	73.25%	8.45%
Found:	73.30%	8.71%

Example 31



Using 0.5 g of 10% palladium-carbon, 3.2 g of 1-(3,4-dibenzyloxyphenyl)-1,8-nonanedione was catalytically reduced in a mixture of 50 ml of ethanol and 1.5 ml of an aqueous 5% perchloric acid solution at room temperature and under atomospheric pressure until the absorption of hydrogen stopped. After the reaction was over, the catalyst was filtered off and the filtrate was

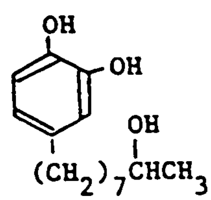
concentrated under reduced pressure. The residue was applied to silica gel (50 ml) column chromatography and eluted with a mixture of toluene and ethyl acetate (4 : 1). The crystals thus obtained were recrystallized from a mixture of toluene and n-hexane to provide 1-(3,4-dihydroxyphenyl)-8-nonanone.

Melting point 73 - 75°C.

Elemental analysis for $C_{15}H_{22}O_3$:

	C	H
Calculated:	71.97%	8.86%
Found:	71.91%	9.12%

Example 32



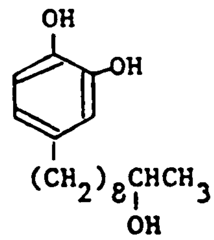
By following the same procedure as in Example 31 using 780 mg of 1-(3,4-dibenzyloxyphenyl)-1,8-nonanediol, 210 mg of 1-(3,4-dihydroxyphenyl)-8-nonanol was obtained.

Melting point 5S - 61°C.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS, ppm):

1.0-1.8(15H), 2.48(2H), 3.84(1H), 6.5-6.9(3H)

Example 33

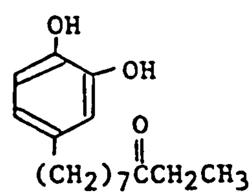


By following the same procedure as in Example 31 using 1 g of 1-(3,4-dibenzyloxyphenyl)-1,9-decanediol, 340 mg of 1-(3,4-dihydroxyphenyl)-9-decanol was obtained. Melting point 43 - 46°C.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS, ppm):

1.05-1.8(17H), 2.50(2H), 3.86(1H), 6.5-6.9(3H).

Example 34

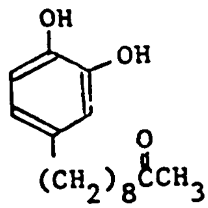


By following the same procedure as in Example 31 using 2 g of 1-(3,4-dibenzyloxyphenyl)-1,8-decanedion as a raw material, 200 mg of 1-(3,4-dihydroxyphenyl)-8-decanone was obtained. Melting point 76 - 78°C.

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS, ppm):

1.04(3H), 1.0-1.8(10H), 2.2-2.6(6H), 6.5-6.9(3H).

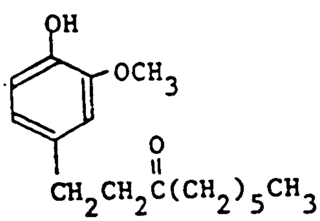
Example 35



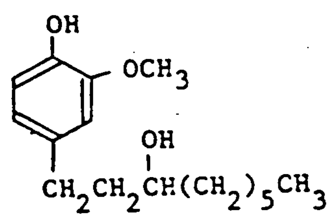
By following the same procedure as in Example 1 using 1.02 g of 1-(3,4- dibenzyloxyphenyl)-1-decen-9-one as a raw material, 450 mg of 1-(3,4-dihdyroxyphenyl)-9-decanone was obtained. Melting point 74 - 76°C.

Nuclear magentic resonance spectra (in $CDCl_3$, TMS, ppm): 1.05-1.8(12H), 2.1(3H), 2.3-2.52(4H), 6.5-6.8(3H).

Example 36



(a)



(b)

By following the same procedure as in Example 4 using 1.2 g of 1-(4-benzyloxy-3-methoxyphenyl)-1-nonen-3-one as a raw material, 660 mg of 1-(4-hydroxy-3-methoxyphenyl)-3-nonanone (a) as an oil and 120 mg of 1-(4-hydroxy-3-methoxyphenyl)-3-nonanol (b) as an oil were obtained.

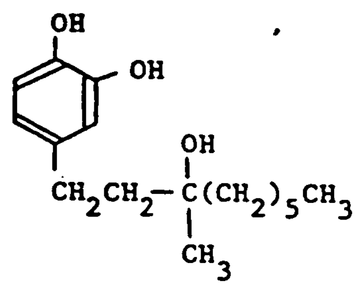
Nuclear magnetic resonance spectra (in $CDCl_3$, TMS, ppm) of compound (a):

0.9(3H), 1.0-1.8(8H), 2.4(2H), 2.5-3.0(4H), 3.88(3H), 6.5-7.0(3H)

Nuclear magnetic resonance spectra (in $CDCl_3$, TMS, ppm) of compound (b):

0.9(3H), 1.0-2.0(12H), 2.5-2.8(2H), 3.4-3.8(1H), 3.88(3H), 6.6-7.0(3H).

Example 37

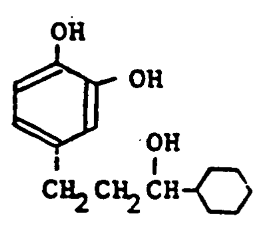


By following the same procedure as in Example 1 using 1.4 g of 1-(3,4-dibenzyloxyphenyl)-3-methyl-3-nonanol, 0.7 g of 1-(3,4-dihdyroxyphenyl)-3-methyl-3-nonanol was obtained. Melting point 81 - 83°C.

Elemental analysis for $C_{16}H_{26}O_3$:

	C	H
Calculated:	72.14%	9.84%
Found:	71.96%	10.06%

Example 38



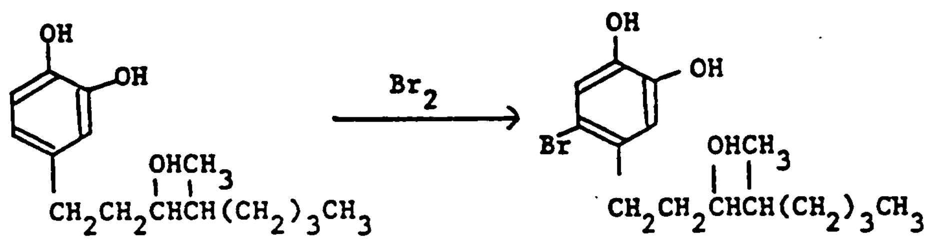
By following the same procedure as in Example 1 using 0.2 g of 3-(3,4-dibenzyloxyphenyl)-1-cyclohexyl-

1-propanol was obtained. Melting point 118 - 119°C.

Elemental analysis for $C_{15}H_{22}O_3$:

	C	H
Calculated:	71.97%	8.86%
Found:	71.85%	8.95%

Example 39



To a solution of 0.5 g of 1-(3,4-dihydroxyphenyl)-4-methyl-3-octanol obtained in Example 1 in 20ml of acetic acid was added dropwise a mixture of 0.37 g of bromine and 2 ml of acetic acid and after the color of bromine disappeared, the solvent was distilled off under reduced pressure. The residue thus formed was extracted with ethyl acetate. The extract was washed with water, dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressure. The residue was applied to silica gel column chromatography and eluted with a mixture of toluene and ethyl acetate (2 : 1) to provide 0.5 g of 1-(2-bromo-4,5-dihydroxyphenyl)-4-methyl-3-octanol.

Melting point 68 - 71°C.

Elemental analysis for $C_{15}H_{23}O_3Br$

	C	H	Br
Calculated:	54.39%	7.00%	24.12%
Found:	54.12%	7.12%	24.40%

Example 40

(Tablet)

11-(3,4-Dihydroxyphenyl)-1-undecanol (hereinafter, is referred to as "ALT-118")	50 mg
Lactose	113 mg
Cone starch	28 mg
Hydroxypropyl cellulose	4 mg
Calcium carboxymethyl cellulose	4 mg
Magnesium stearate	1 mg
total	200 mg

After uniformly mixing 50 g of ALT-118, 113 g of lactose and 28 g of cone starch, 40ml of a 10% (w/v) aqueous solution of hydroxypropyl cellulose was added to the mixture and the resultant mixture was granulated by a wet granulation method. The granules thus obtained were mixed with 4 g of calcium carboxymethyl cellulose and 1 g of magnesium stearate and the mixture was press-tableted into tablets (200 mg per tablet).

Example 41

(Capsule)

ALT-118	50 mg
Crystalline cellulose	20 mg
Crystalline lactose	129 mg
Magnesium stearate	1 mg
total	200 mg

The above components each in an amount 1000 times the foregoing amount were mixed and then filled in gelatin capsule to provide capsules (200 mg per capsule).

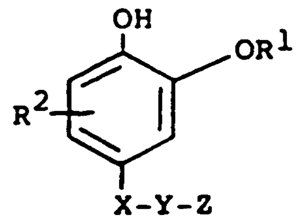
Example 42

(Inhalation)

After dissolving 0.1 g of ALT-118 in about 90 ml of mixture of ethanol, propylene glycol and purified water (30:10:60 in weight ratio), the volume of the solution was adjusted to 100 ml using the aforesaid mixture and 10 ml each of the solution was filled in a definite container followed by sealing to provide an inhalation.

CLAIMS:

1. A catechol derivative represented by the formula



wherein R^1 represents a hydrogen atom or a C_1 to C_5 alkyl group; R^2 represents a hydrogen atom or a halogen atom; X represents a straight chain or branched alkylene group having 1 to 15 carbon atoms or a vinylene group; Y represents a carbonyl group or a group represented by $-\overset{OR^3}{\underset{R^4}{C}}-$ (wherein R^3 and R^4, which may be the same or different, each represents a hydrogen atom or a C_1 to C_5 alkyl group) and Z represents a hydrogen atom, a straight chain or branched alkyl group having 1 to 15 carbon atoms or a cycloalkyl group; the sum of the carbon atoms of said X and Z being at least 3.

2. One or more of the following compounds according to claim 1: 11-(3,4-dihydroxyphenyl)-1-undecanol;

11-(4-hydroxy-3-methoxyphenyl)-1-undecanol;

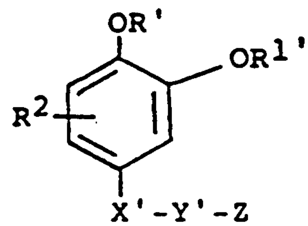
10-(3.4-dihydroxyphenyl)-1-decanol;

1-(3,4-dihydroxyphenyl)-3-undecanol;

9-(3,4-dihydroxyphenyl)-2-nonanone;

1-(3,4-dihydroxyphenyl)-4-methyl-3- octanol.

3. A process of producing a catechol derivative according to claim 1 which comprises reducing and/or hydrolizing, or halogenating a compound represented by general formula (II)



(II)

wherein R' represents an easily removable protective group for hydroxyl; $R^{1'}$ represents an easily removable protective group for hydroxyl or a C_1 to C_5 alkyl group; R^2 is as defined in claim 1; X' represents a straight chain or branched alkylene group having 1 to 15 carbon atoms, an alkenylene group represented by formula $-(CH_2)_{m'}CH{=}CH-$ (wherein m' is 0 or an integer of 1 to 13), or a group represented by formula $-\overset{O}{\overset{\|}{C}}-(CH_2)_{m''}$ or $-\overset{OH}{\overset{|}{C}}H-(CH_2)_{m''}-$ wherein m" is an integer of 1 to 14, said $-(CH_2)_{m'}-$ and $-(CH_2)_{m''}-$ in the above formulae being straight chain or branched; Y' represents a carbonyl group or a group represented by $-\underset{R^4}{\underset{|}{\overset{OR^{3'}}{\overset{|}{C}}}}-$ ($R^{3'}$ and R^4, which may be the same or different, each representing a hydrogen atom or a C_1 to C_5 alkyl group with $R^{3'}$ optionally being instead of a protective group for hydroxyl; and Z is as defined in claim 1; the sum of the carbon atoms of said X' and Z being at least 3.

4. A process according to claim 3 which involves the reduction of a carbonyl group in the compound of formula (II) into a hydroxymethylene group or a methylene group, the reduction of an alkenylene group into an alkylene group, the removal of the protective group for hydroxyl, and the halogenation of the benzene group, these reactions being performed in any order.

5. A process according to claim 3 wherein the reduction of a carbonyl group in the compound of formula (II) into a hydroxymethylene group or a methylene group, the reduction of an alkenylene group into an alkylene group, and the removal of the protective group for hydroxyl are performed simultaneously.

6. A process according to claim 5 wherein the reductiongs and the removal of the protective group are performed by catalytic reduction, e.g. using a palladium-carbon catalyst.

7. A pharmaceutical composition containing a compound according to claim 1 or 2 in a pharmaceutical carrier.

8. A compound of formula (II) as defined in claim 3.

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PARTIAL EUROPEAN SEARCH REPORT
which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application number
EP 84 30 3257

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.)
X	JOURNAL OF THE CHEMICAL SOCIETY, Perkins Transactions 1, volume 23 1972, pages 3001-3006 LETCHWORTH, Herts (GB) H.D. LOCKSLEY et al.: "Pungent Compounds. Part I. An improved synthesis of the paradols (alkyl 4-hydroxy-3-methoxyphenethyl ketones) and an assessment of their pungency" * whole document * --	1	C 07 C 39/11 C 07 C 37/00 C 07 C 49/245 C 07 C 43/23 C 07 C 41/26 C 07 C 41/30 A 61 K 31/05 A 61 K 31/12 C 07 C 45/29 C 07 C 45/68
X	CHEMICAL ABSTRACTS, volume 70, no. 21, May 26, 1969, page 297 abstract 96341f COLUMBUS, OHIO (US) G. SCHILL et al.: "Rotaxane compounds" & Justus Liebigs Ann.Chem. 1969, 721, 53-74(Ger). * abstract * --	1,2	
			TECHNICAL FIELDS SEARCHED (Int. Cl.)
			C 07 C 39/00

INCOMPLETE SEARCH ./.

The Search Division considers that the present European patent application does not comply with the provisions of the European Patent Convention to such an extent that it is not possible to carry out a meaningful search into the state of the art on the basis of some of the claims.
Claims searched completely: 1-8
Claims searched incompletely: 9-10
Claims not searched:
Reason for the limitation of the search:

Contrary to the Rule 29 (6) of the Implementing Regulations to the Convention on the Grant of European Patents of 5 October 1973

Place of search	Date of completion of the search	Examiner
THE HAGUE	26-09-1986	KLÅG

CATEGORY OF CITED DOCUMENTS

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